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ROYAL COMMISSION OF INQUIRY INTO CERTAIN  
DEATHS AT THE HOSPITAL FOR SICK CHILDREN AND  
RELATED MATTERS.

Hearing held in Court Room 20  
Court House  
361 University Avenue  
Toronto, Ontario

The Honourable Mr. Justice S.G.M. Grange

Commissioner

P.S.A. Lamek, Q.C.

Counsel

E.A. Cronk

Associate Counsel

Thomas Millar

Administrator

Transcript of evidence  
for

July 6th, 1983

VOLUME 8

## OFFICIAL COURT REPORTERS

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ROYAL COMMISSION OF INQUIRY INTO CERTAIN  
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Court House, 361 University  
Avenue, Toronto, Ontario, on  
Wednesday the 6th day of July,  
1983.

THE HONOURABLE MR. JUSTICE S.G.M. GRANGE - Commissioner  
THOMAS MILLAR - Administrator  
MURRAY R. ELLIOT - Registrar

APPEARANCES:

E.A. CRONK	Commission Counsel
D. HUNT ) L. CECCHETTO)	Counsel for the Attorney- General and Solicitor General of Ontario (Crown Attorneys and Coroner's Office)
I.G. SCOTT, Q.C.) I.J. ROLAND )	Counsel for The Hospital for Sick Children
R. DEVINS ) R. BATTY )	
D. YOUNG	Counsel for The Metropolitan Toronto Police
K. CHOWN	Counsel for numerous Doctors at The Hospital for Sick Children
F. KITELY	Counsel for the Registered Nurses' Association of Ontario and 35 Registered Nurses at The Hospital for Sick Children

(Cont'd)








APPEARANCES:

H. SOLOMON	Counsel for the Ontario Association of Registered Nursing Assistants
W.A. BOGART	Counsel for Susan Nelles - Nurse
G.R. STRATHY) P. RAE )	Counsel for Phyllis Trayner - Nurse
C. BUHR	Counsel for Sui Scott - Nurse
B. KNAZAN	Counsel for Mrs. M. Christie - R.N.A.
J.A. OLAH	Counsel for Janet Brownless (Vereecken) - R.N.A.
S. LABOW	Counsel for Mr. & Mrs. Gosselin, Mr. & Mrs. Gionas, Mr. & Mrs. Inwood, Mr. & Mrs. Turner, and Mr. & Mrs. Lutes (parents of deceased children)
F.J. SHANAHAN	Counsel for Mr. & Mrs. Dominic Lombardo (parents of deceased child Stephanie Lombardo)
W.W. TOBIAS	Counsel for Mr. & Mrs. Hines, (parents of deceased child Jordan Hines)



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---Upon commencing at 10:00 a.m.

DR. GRAHAM ELLIS, Resumed

THE COMMISSIONER: Mr. Buhr, have  
I called on you?

MR. BUHR: I have no questions,  
Mr. Commissioner.

THE COMMISSIONER: Is there anyone  
here for Mrs. Christie?

MS. GOODMAN: No questions.

THE COMMISSIONER: Mr. Young, do  
you have any questions?

MR. YOUNG: I do not have any  
questions, Mr. Commissioner.

THE COMMISSIONER: Miss Chown?

MS. CHOWN: No questions.

THE COMMISSIONER: We are doing  
well, are we not? I think I should start at  
about a quarter to 10:00 and then I will really get  
through this. Mr. Roland?

MR. ROLAND: I hate to disappoint  
you, Mr. Commissioner, but I have no questions  
either, sir.

THE COMMISSIONER: All right.  
Mr. Labow?

MR. LABOW: I have no questions and







1  
2 Mr. Shanahan also informed me that he would not have  
3 any questions.

4 THE COMMISSIONER: All right. We  
5 are doing well. Mr. Scott?

6 EXAMINATION BY MR. SCOTT:

7 Q. Dr. Ellis, I would just like to  
8 ask you one or two questions in two areas.

9 First of all, Mr. Strathy yesterday  
10 asked you some questions about the testing you do  
11 and the record books you maintain of those tests.  
Do you recall that?

12 A. Yes.

13 Q. And in that connection he  
14 asked you if you were able to determine from an  
15 examination of your books the number of tests that  
16 would have been at the toxic level, which is the  
17 way he put it. Do you remember that? He asked you,  
18 following that, if you could at some time give to  
19 the Inquiry the percentage of tests, over a given  
period, at the toxic level. Do you remember that?

20 A. Yes, I think that was one of  
21 his questions, but I thought he had backed off from  
22 that.

23 Q. Well, just to be sure he backed  
24 off, we are going to deal with it. I take it that  
25





1  
2 the toxic level is the level above the therapeutic  
3 level?

4 A. I don't know quite how he  
5 defined it. I indicated that I had searched those  
6 books on a previous occasion for levels greater than  
7 5 and had presented a list to the Preliminary  
8 Hearing.

9 Q. Let me put this to you. The  
10 so-called therapeutic level of digoxin, that level,  
11 I take it, is determined arbitrarily by a literature  
12 search?

13 A. Yes.

14 Q. And a level above that  
15 therapeutic level is what is sometimes called the  
16 toxic level?

17 A. Yes.

18 Q. Am I right?

19 A. Yes.

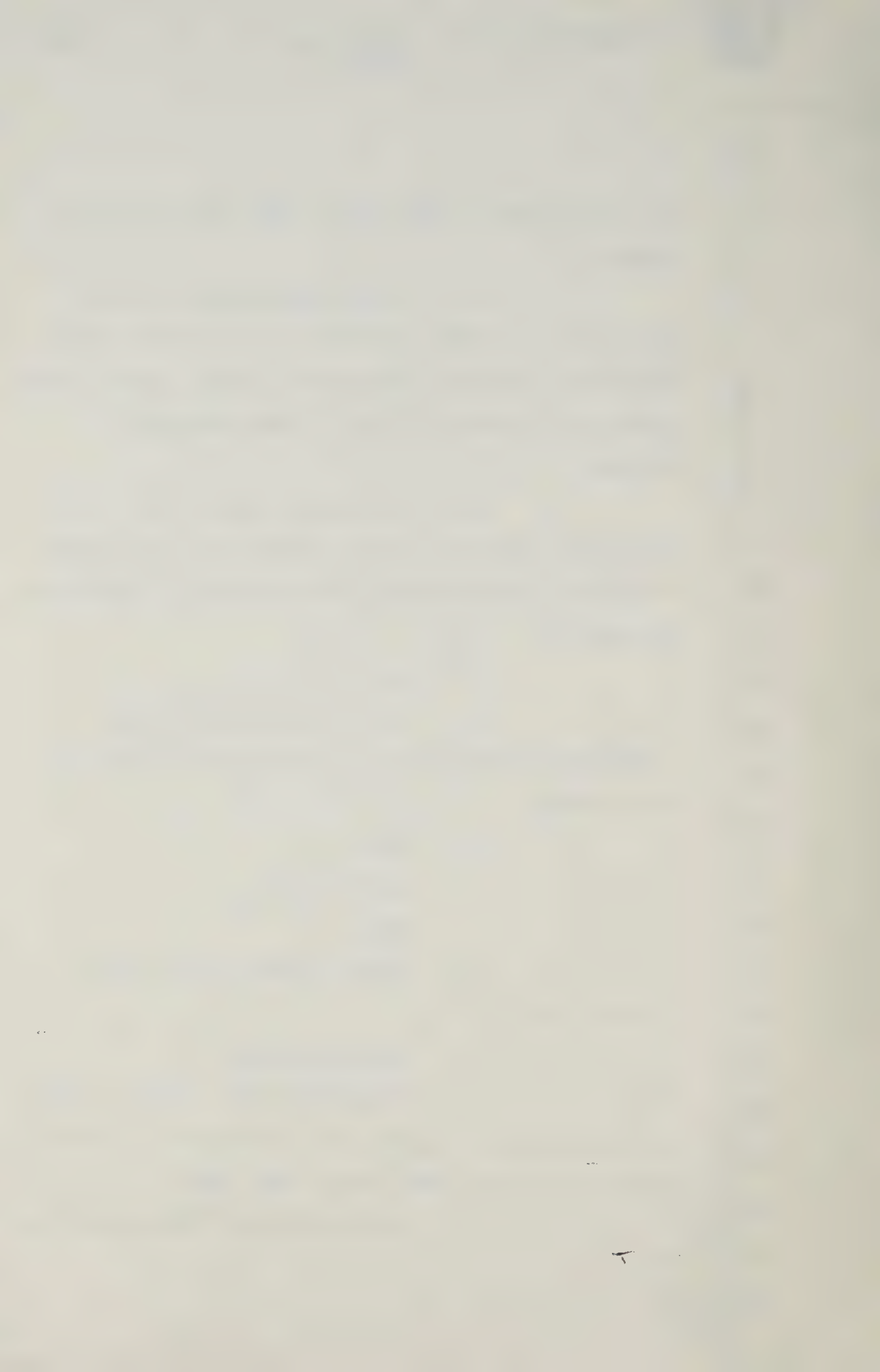
20 Q. Simply because it is above a  
21 certain ---

22 A. Threshold level.

23 Q. Threshold level. Now, I take  
24 it that you as a chemist have no capacity to deter-  
25 mine whether any level is in fact toxic?

A. On the clinical indications that







1  
2 the patient may be showing at that particular time,  
3 I have no knowledge of those clinical symptoms.

4 Q. Would it be correct to say  
5 that whether a digoxin level is in fact toxic is  
6 something that is not for your expertise?

7 A. Yes.

8 Q. It is for the expertise of the  
9 clinician on the spot?

10 A. Yes.

11 Q. Now, Mr. Hunt asked you some  
12 questions about the differences between your disci-  
13 pline and the discipline of a forensic chemist. I  
14 do not intend to get into that interesting question  
15 but I simply want to ask you this. You heard

16 Mr. Cimbura's evidence?

17 A. Yes.

18 Q. And you heard him describe  
19 RIA testing for digoxin, did you?

20 A. Yes.

21 Q. Was there anything in the RIA  
22 testing for digoxin that he described that was  
23 foreign to your expertise in terms of either theory  
24 or practice?

25 A. Nothing that immediately comes  
to mind.







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Q. Is the RIA testing for digoxin  
that he was doing parallel to the RIA testing for  
digoxin that you traditionally do in the Hospital  
for Sick Children?

A. Similar in many ways, yes.

MR. SCOTT: Those are all the  
questions I have, thank you, Dr. Ellis.

MS. CRONK: Mr. Commissioner, we  
were supplied last night with a copy of the articles  
which, as I understand it, Dr. Ellis referred to  
during the course of cross-examination by Miss Symes  
yesterday and I propose that they be marked now as  
exhibits.

Perhaps, Dr. Ellis, just to ensure  
that I do have the right articles you can let me  
know if I refer to any that you did not refer to,  
but it is my understanding that these are the three  
that you referred to with Miss Symes.

The first, Mr. Commissioner, is  
entitled "Myocardial vs Serum Digoxin Concentrations  
in Infants and Adults", published in May 1982,  
co-authored by Park, Ludden and others.

RE-EXAMINATION BY MS. CRONK:

Q. Is that one of the articles to  
which you referred, Dr. Ellis?





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A. Was that the third article to  
which I referred?

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THE COMMISSIONER: Where was it  
published?

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MS. CRONK: Q. Would you look at that  
article, Dr. Ellis, and just let us know where that  
was published and if that was one of the ones that  
you referred to?

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A. Yes, the "Myocardial vs Serum  
Digoxin Concentrations..."?

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14

Q. Yes.

A. The American Journal of  
Diseases in Children or Childhood - I think it is  
Children - Volume 136, May, 1982.

15

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Q. Thank you.

Could that be marked then,  
Mr. Commissioner, as the next exhibit, please.

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THE COMMISSIONER: Exhibit 19.

---EXHIBIT NO. 19: Article entitled "Myocardial  
vs Serum Digoxin Concentrations  
in Infants and Adults".

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MS. CRONK: Q. And the next one  
that I have before me is entitled "Correlation of  
Antemortem and Postmortem Digoxin Levels".

Do you have that before you?







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A. Yes.

Q. Can you tell the Commissioner by whom it was published, when and where?

A. This was in the Journal of Forensic Science, Volume 23, page 329 to 334, 1978. The authors are V-o-r-p-a-h-l, T. E., (I do not know how it is pronounced) and Coe, C-o-e, J. I.

MS. CRONK: Could that be marked, sir, as the next exhibit, please?

THE COMMISSIONER: Exhibit 20.

---EXHIBIT NO. 20: Article entitled "Corrélacion of Antemortem and Postmortem Digoxin Levels".

MS. CRONK: Q. The third article that I have, Dr. Ellis, is entitled "Post-Mortem Digoxin Levels-Two Unusual Case Reports".

Could you tell the Commissioner again who the authors of that report were and where it was published and when?

A. Yes, the authors are Dickson, S.J. and Blazey, B-l-a-z-e-y, N.D. And this was in the Forensic Science, Volume 9, 1977, page 145 to 150.

Q. Thank you.

Again, sir, could that be marked as







1  
2 the next exhibit?

3 THE COMMISSIONER: Exhibit 21.

4  
5 ---EXHIBIT NO. 21: Article entitled "Post-Mortem  
6 Digoxin Levels-Two Unusual  
Case Reports" by S.J. Dickson  
and N.D. Blazey.

7 MR. ROLAND: Excuse me,  
8 Mr. Commissioner, could you advise us what exhibit  
9 numbers these are?

10 THE COMMISSIONER: Yes, 19, 20 and  
11 21 respectively.

12 MS. CRONK: One other question,  
13 Mr. Commissioner, with respect to the last article  
14 that we have just marked.

15 Q. Dr. Ellis, there is some hand-  
16 writing that appears on the face page and throughout  
17 the copy of the article that I have. Can you identify  
that handwriting for us?

18 A. I did mark quite a few of  
19 these articles. I think it is probably mine.

20 Q. Thank you.

21 The last exhibit, Mr. Commissioner,  
22 at Mr. Strathy's request I have copies made of a  
23 reduced version of this chart, and if it will be  
24 of any utility to anyone in reviewing the transcript  
25 I propose that it be marked as the next exhibit.





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2 THE COMMISSIONER: Exhibit 22.

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4 ---EXHIBIT NO. 22: Copy of Chart produced by  
Ms. Cronk.

5 MS. CRONK: Thank you.

6 Q. Dr. Ellis, just a few questions  
7 if I may. You will recall that yesterday during  
8 the cross-examination conducted by Ms. Symes your  
9 attention was drawn to Exhibit 14 which, as you may  
10 recall, is the publication produced by Antibodies Inc.  
11 of California concerning its antiserum, the one that  
12 is used by you in the hospital to conduct RIA  
digoxin assays. Do you recall that?

13 A. Yes.

14 Q. It was suggested to you, and  
15 as I understood your response to the questions put  
16 to you by Ms. Symes, that the digoxin antiserum  
17 produced by Antibodies Inc. and as referred to in  
18 that publication was designed for ante mortem  
19 sampling for digoxin. Do I have that correctly?

20 A. I believe that to be the case.  
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Q. All right.

A. Is there any indication other-  
wise here?

Q. Well, I'll come to that in a  
moment, Dr. Ellis. I just want to be clear as to  
what I understood your evidence to be yesterday.

Do you recall Miss Symes asking you  
and directing questions to you as to what the purpose  
and design intent was of that antibody?

A. Yes.

Q. Do you recall that?

A. Yes.

Q. And as I recall your answers  
to those questions, you indicated that they were  
designed for ante mortem digoxin sample.

A. Yes.

Q. All right. Now, can you tell  
me, Dr. Ellis, specifically the point that you now  
raise, in any of the literature or promotional  
materials that have ever been provided to you by  
Antibodies Inc. with respect to that antiserum or,  
indeed, any of the conversations that you've had  
with the Quality Control Manager of that company  
or others associated with the company, was any  
indication given to you to suggest or to indicate





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that the antiserum was not suitable for post mortem testing on plasma or serum samples?

A. No.

Q. Thank you.

And as I understood your evidence yesterday as well, Dr. Ellis, you told Miss Symes that, in your view, it would take several months to adapt a method at the Hospital to conduct post mortem testing on certain kinds of samples.

Do you recall that evidence?

A. Yes. I think it may well take several months.

Q. All right.

I would like to be clear, and I may well have heard it correctly yesterday, Dr. Ellis, but I would like to be clear in my own mind, were you drawing a distinction, in answering that question, between particular types of samples or were you referring to samples at large?

A. I think we have plenty of experience in analyzing regular serum samples, but it is just the other samples, other than those, that would require some work to be done, I feel.

Q. Well, all right. More specifically, can you help me with this: In your







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view, would it take a period of several months to adapt the RIA method that is being used in the Hospital to test post mortem tissue samples?

5

A. I think it could well take several months, yes.

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8

Q. And similarly, to conduct post mortem digoxin assays on serum samples, would that also take several months to adapt your method?

9

10

A. Well, it could be used for post mortem serum samples.

11

Q. As it stands today?

12

A. Just in the same way that regular serum samples are used.

13

14

Q. All right.

15

And what is the situation with respect to plasma samples?

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A. But the interpretation may be slightly different in the results you obtain.

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Q. I appreciate that, Dr. Ellis, but in terms of the technical capacity of the methodology as it now exists in the Hospital to do post mortem digoxen assays on serum samples, is that something that could be done today without modifying the system?

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A. Well, that is something that we





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have been requested to do, and are doing currently  
without a modified system.

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Q. Thank you.

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And similarly, what is the situation  
with respect to plasma samples?

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A. Plasma and serum, I would  
equate those two.

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Q. All right. So, am I correct,  
then, that, in your view, no modification of the  
methodology was necessary at the Hospital to conduct  
post mortem tests on those two kinds of samples?

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A. We undertook no studies when  
we were requested to analyze post mortem serum  
samples because of the similarity in many respects  
between pre and post mortem serum samples. We did  
think, I think, when we initially agreed to do these,  
that it would be for a very short time only. We  
hadn't really anticipated that we would still be  
analyzing these samples.

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Q. As you sit here today, you are  
still doing that; is that correct?

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A. We are doing that, yes. Yes.

Q. And you keep referring, Dr.

Ellis, to serum. Are you, in that context, using  
serum interchangeably with plasma?







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A. Yes.

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Q. Thank you.

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In your judgment, Dr. Ellis, having regard to your experience in conducting radio-immunoassays for digoxin, do you have any misgivings in using the methodology or technique as it has been developed in the Hospital for the purpose of conducting post mortem digoxin assays on blood or serum samples?

10

A. On blood or serum --

11

Q. Yes.

12

A. -- or on plasma and serum?

13

Q. I'm sorry, plasma and serum; you're quite right.

14

A. Do I have any major misgivings in what respect?

16

Q. Well --

17

A. In respect of interpretation of the numbers that would be produced?

18

19

Q. Well, let's be clear about this.

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As I understood it, the burden of your evidence before the Commissioner has been that it is not part of your function to interpret the results that come off of a particular assay reading; is that correct?

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THE COMMISSIONER: I think you are concerned about -- I think your question is the analysis, the result.

MS. CRONK: That's right.

Well, let me rephrase the question then, Mr. Commissioner. I apologize if it has been confusing, Dr. Ellis.

Q. Based on your experience as a biochemist in conducting radioimmunoassays, digoxin assays, in the Hospital, do you have any misgivings, as a biochemist, in terms of the technical capability of the methodology that is now in place in the Hospital for the purposes of running digoxin assays on post mortem serum or plasma samples?

A. No major misgivings, no, in that the protein composition of the pre and post mortem samples is essentially similar. The electrolyte composition is essentially similar.

Q. And I take it, sir - and perhaps you can tell me, would you have any misgivings about using the system to conduct a post mortem tissue --

A. Major misgivings, yes.

Q. Major misgivings, thank you.





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And you told Mr. Strathy, as I recall it, that, in order to moderate the radioimmunoassay technique presently available in the Hospital for the purposes of conducting post mortem digoxin assays on tissue samples, that would require an addition to the modification of the system itself and, in your view, it would also require an extensive literature review; is that correct?

A. Yes, very much so.

Q. And I believe, if I understood your evidence correctly, that you also told him that you, if you were asked or required to modify the system for that purpose, would wish to speak to those persons whom you knew had experience in doing digoxin assays on tissue samples; is that correct?

A. That may cut down some of the time involved to do that, yes.

Q. Would that, in your view, be a desirable step to take if you were modifying your system for that purpose?

A. Yes.

Q. And in that context, would you consider it appropriate to discuss with Mr. Cimbura his experience in conducting those kinds of tests?







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A. Yes, I think it would, Mr.

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Cimbura or other people, too.

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Q. And I believe, again if I

5

understood your evidence correctly, that you also

6

told Mr. Tobias, in his cross-examination of you

7

yesterday, that, in order to use the materials

8

supplied by Antibodies Inc., the antiserum for those

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kinds of post mortem tests, the kit would have to

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be used with - and at least this is what my note

11

of your evidence indicates - a lot of caution and a

12

lot of tests.

Do you recall giving that evidence?

13

A. A lot of caution, yes.

14

Q. Yes. All right.

15

And, again in that regard, were you

16

referring to particular kinds of samples that would

17

be tested on a post mortem basis or were you refer-

18

ring to samples at large?

19

A. Samples in general, in view

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of the fact that tissues might have binding sub-

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stances present that might interfere with the

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simple radioimmunoassay.

Q. Were you referring as well to

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plasma or serum samples?

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A. I think it would depend. You're

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talking about post mortem plasma?

Q. Yes, I am.

A. Yes. Well, it is difficult to generalize, really, because if a child dies and a blood sample is taken ten minutes after death from an arm, then that sample is a post mortem sample essentially.

Q. Yes.

A. But it is really very close to the time when the patient was alive.

If, on the other hand, you go to perhaps 24 hours afterwards, when an autopsy has been performed, then you are in a kind of different situation.

Q. In your view, doctor, then, if you were to conduct or modify your system for post mortem digoxin assays on plasma or serum, would it require that you exercise the same degree of caution and the same degree of multiple tests as you suggested it would to use the Antibodies Inc. anteserum for tissues?

A. I think so, because there may be, particularly if the blood sample is taken from the heart, there might perhaps have been some decomposition, a partial decomposition of the heart







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tissue.

Q. Yes.

A. And this might perhaps have released certain proteins from the heart tissue that might possibly interfere with the assay.

All these things would have to be tested for.

Q. All right.

And again, dealing now for the moment with just post mortem testing on tissue samples, as I understood your responses to Mr. Tobias, you indicated, again in modifying the system, that it would have to be modified potentially in several respects, perhaps to include an extraction process.

A. Yes.

Q. Do you recall giving that evidence?

A. Yes.

Q. Did you have in mind, in giving that response, the kind of extraction process that we have heard is utilized by Mr. Cimbura at the Centre?

A. I think there are several extraction processes for the purpose of purifying the sample that one is dealing with.















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Q. All right.

A. And all of those would have to be evaluated appropriately.

Q. In your view then, Dr. Ellis, if one were to modify or develop a radioimmunoassay technique for the purposes of conducting post mortem tests on tissue samples, would an extraction process be a proper and desirable ingredient in that test?

A. I think, in many cases, it may be called for, yes.

Q. Thank you.

And I believe you indicated as well, in answer to a number of questions put by various counsel, that you were not familiar with, and had not used, either the Beckman kit or the Beckman antibody; is that correct?

A. That's correct.





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Q. Would I be correct then in taking from that answer, Dr. Ellis, that you are not familiar with the restrictions, if any, that the Beckman Company attach to their RIA kit for the purposes of conducting digoxin assays?

A. That is correct.

Q. And just one final point on that, Dr. Ellis, you may recall that in the cross-examination conducted by Mr. Bogart yesterday he directed to you questions regarding the quantity of whole blood that would be necessary to result in a sufficient quantity of serum, or plasma, for the purposes of conducting a digoxin assay. Do you recall that discussion?

A. Yes.

Q. Can you help me Dr. Ellis, during the period July 1980 to March 1981, did you in your Laboratory in fact conduct digoxin assays on whole blood?

A. No.

Q. Do you now?

A. No.

Q. In the intervening period between March '81 up to today's date as we sit here, are any digoxin assays conducted on whole blood in the Hospital to your knowledge?







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A. To my knowledge, no.

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Q. Thank you. You may recall as well in addition to that particular area, Mr. Bogart during his cross-examination drew your attention to a discussion that you and I had had in your evidence in chief with respect to the drugs that may or may not have been tested by Antibodies Inc. for cross-reactivity, or the absence of cross-reactivity with the anti-serum that that company provides. He referred you in that regard to furosemide, propranolol, if I am pronouncing it correctly?

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A. Propranolol.

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Q. I am not going to try it again, Dr. Ellis, and the third quinidine, do you recall that discussion?

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A. Yes.

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Q. First of all, can you tell me when you refer in that context to anti-serum, is that word interchangeable for the purposes in this context with the antibody that is supplied by Antibodies Inc.?

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A. Yes.

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Q. Now, I was left with some confusion undoubtedly through my own error, as to what your evidence was in that respect. As I





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understood what you told Mr. Bogart, you said the supplier could not test those drugs for cross-reactivity with the anti-serum provided by Antibodies Inc., do I have that correctly?

A. The supplier could not have tested for those drugs?

Q. Yes.

A. No, I don't think I said that.

Q. That is why I want to clarify it, Dr. Ellis, because I am uncertain in my own mind. Technically, could those drugs have been tested for cross-reactivity by Antibodies Inc. as the supplier of that antibody?

A. Yes, they could.

Q. To your knowledge, was that done?

A. To my knowledge, I don't have any information on that.

Q. Thank you.

A. On all the specifics that you mentioned, but for the reasons that I explained yesterday there would be a logical reason why they wouldn't necessarily test all those drugs. Simply because the interference that was alluded to several weeks ago I think where a large number of drugs were mentioned. I think Mr. Cimbura was asked about this.





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Where there were a very large number of drugs interfered with his assay, to his knowledge, and basically the point I was trying to make was you could divide that large group of drugs into two groups.

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Q. Yes.

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A. One of which if you took the drug and added it to your assay system you could get interference. For example, if you took digitoxin you could get interference in your assay system.

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The other group of drugs are drugs which if co-administered with digoxin to a patient, the true digoxin of that patient may increase as a result of the co-administration of that drug, and I believe that one such drug is quinidine, for example. So there is no structural similarity, to my knowledge, in the chemical structure of quinidine and digoxin and there would be no indication for assaying it in the assay system, in the radioimmunoassay system. So I was just trying to clarify that rather confused area.

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Q. Thank you, Dr. Ellis. To be fair to you, as I understand what you have just said, the issue as to whether or not there was any utility, or whether it was desirable for any reason to test







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on the assay those three drugs for cross-reactivity  
is one issue?

A. Yes.

Q. The other issue is whether or  
not technically it could be done to determine whether  
or not they were in fact cross-reactive. Am I correct  
in that?

A. Yes. You could technically take  
every drug in the pharmacopeia or whatever solution  
you cared to make, assuming it dissolved, and put it  
in the assay system if you so wished.

Q. Thank you. If a physician or  
a biochemist had any reason to inquire into the  
cross-reactivity of any drug to the digoxin antibody,  
technically a cross-reactivity test could be run in  
respect of that drug, is that correct?

A. Yes, assuming this was soluble  
under the conditions that this dissolved in the  
solution.

Q. So for example in respect of  
any patient, a hypothetical patient, if you knew that  
certain drugs had been prescribed to that patient  
it would technically be possible to run a test on  
each and every one of those drugs for cross-reactivity  
of the digoxin antibody that is in use in the  
hospital?





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A. I think in general one could

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say that.

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Q. And you may recall as well, Dr.

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Ellis, that during the cross-examination of you by

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Mr. Strathy yesterday, your attention was drawn to

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the recent studies and the recent published articles

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concerning what has been called in this courtroom

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"Substance X", do you recall that?

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A. Yes.

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Q. And as I understood the exchange

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yesterday it was suggested to you that in light of

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those recent studies there is difficulty in relying

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on the radioimmunoassay technique for digoxin testing

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on very young children. Do you recall that?

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A. Yes.

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Q. As I recall it as well Mr. Strathy

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questioned you with respect to, as Mr. Scott referred

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to earlier this morning, the number of patients in

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the Hospital between July 1980 and March 1981 that

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were experiencing toxic digoxin levels, do you recall

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that?

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A. Yes.

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Q. And you previously told us that

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in the area, if I have your evidence right, that in

the area of interpretation of results of readings from





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a digoxin assay, levels recorded by the use of the radioimmunoassay technique cannot be regarded in isolation from the clinical history, or the clinical pattern of a particular patient, is that correct?

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A. Yes.

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Q. Would you agree with me, Dr.

Ellis, I am trying to confirm whether or not my understanding of this particular issue is correct, that dealing with the case of very young children as referred to by Mr. Strathy, it is possible for very young children to record on a digoxin assay a level of 2 nanograms per millilitre, 2.5 nanograms per millilitre or higher, yet having regard to their clinical condition not be in the toxic range?

A. Yes, not be in the toxic range, or not show clinical symptoms of toxicity.

Q. Well, let's take it in two parts. Is it possible, based on your experience, dealing again with very young children, for a digoxin level to be recorded of 2 nanograms plus, and yet upon interpretation of those results it could be determined that the particular child was not experiencing toxicity from digoxin?

A. Yes.

MR. SCOTT: Mr. Commissioner, I don't







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mean to interrupt. This is a point of some confusion which I hoped I had cleared up, but perhaps I failed.

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The expression "toxic range" perhaps Miss Cronk can pursue this, is a numbers game. If you are above a

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certain level you are in a toxic range, it has nothing to do with whether it is in fact toxic.

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MS. CRONK: That is my point.

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MR. SCOTT: That is whether it is poisoning somebody.

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MS. CRONK: That is my point, Mr. Commissioner, and perhaps I have expressed it badly.

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THE COMMISSIONER: Is this the right witness to ask that question of?

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MS. CRONK: Well, I am not asking Dr. Ellis for obvious reasons, what his view of an appropriate interpretation would be. The understanding that I took away from the cross-examination conducted by Mr. Strathy yesterday in respect of this matter, I just want to make it very clear if I have it correctly, that as far as Dr. Ellis is concerned that a reading alone from a very young child of 2 or better than 2, is not necessarily indicative of digoxin toxicity.

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THE WITNESS: Is not always associated with clinical signs and symptoms of digoxin toxicity.





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MS. CRONK: Fair enough, fair enough,  
thank you, Dr. Ellis.

Q One final point, Dr. Ellis. You  
will recall yesterday, and again my friend Mr. Scott  
referred to this this morning. Mr. Hunt having a  
discussion with you concerning the distinctions  
between the practice and discipline of a clinical  
biochemist and a forensic biochemist. I wanted just  
to be again clear in my own mind as to what your  
evidence had been in that respect because I thought  
I had understood your evidence on Thursday and I came  
away with some confusion yesterday.

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Am I correct, Dr. Ellis, that you personally have had no experience with the HPLC testing method for digoxin assays?

A. Yes.

Q. Have you had any experience with what has been called the HPLC mass spectrometry technique for digoxin assays?

A. The HPLC --

Q. MS, mass spectrometry. I perhaps am saying that wrong, for digoxin assays?

A. I have not, no, but I don't believe Mr. Cimbura has either. I don't think there is anybody in Canada who has had experience in that.

Q. But in any event, you, sir, have not?

A. No.

Q. Am I correct as well that in the RIA testing and the assays done at the Hospital you have not had experience with what has been referred to as the double antibody system, that is, an antibody used for the purposes of attracting the patient digoxin or the radioactive digoxin and the second antibody used for the purposes of separating the bound digoxin from the unbound digoxin. You have not had experience with the double antibody system?







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A. I have had quite a lot of experience with double antibody systems for assays other than digoxin.

Q. I am sorry, I meant for digoxin assays. So it is correct that for digoxin assays you have not used that kind of a system?

A. Yes.

Q. Thank you.

Similarly, am I correct, Dr. Ellis, that you have had no experience with the creating of a radioimmunoassay technique or indeed any other kind of assay technique purely for the purposes of running digoxin assays, because when you joined the Hospital for Sick Children that technique was already in place. Is that correct?

A. Yes. We have tried modifying it in various ways but essentially we come back to the same point, more or less.

Q. Am I correct then that you have not been required to design and implement a system for digoxin assays, from scratch?

A. No.

Q. Similarly, am I correct, Dr. Ellis, that you have had no experience with adapting your, and by your I mean the RIA assay system that is in use





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at the Hospital, for the purposes of conducting post  
mortem tissue sampling assays?

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A. Yes, I think I indicated this  
before.

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Q. That adaptation has not taken  
place?

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A. Yes. I have not spent a lot of  
time doing that, no.

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MS. CRONK: Thank you. Thank you for  
your patience, Dr. Ellis. I have no further questions,  
Mr. Commissioner, unless you do?

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THE COMMISSIONER: Thank you, Doctor.

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MS. CRONK: Thank you very much, sir.

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Our next witness is Dr. Steven Soldin  
from the Hospital for Sick Children.

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DR. STEVEN SOLDIN, Sworn

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THE COMMISSIONER: Is that a "v" or a  
"ph" in Steven, Doctor?

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THE WITNESS: With a "v".

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THE COMMISSIONER: Thank you.

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DIRECT EXAMINATION BY MS. CRONK:

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Q. Dr. Soldin, I have handed to you  
a copy of your curriculum vitae which was provided to  
me by your Counsel. As I understand it, you were born  
in Johannesburg, South Africa, in October of 1940. Is  
that correct?





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A. That is correct.

Q. And you obtained a Bachelor of  
Science Honours Degree in Chemistry in 1962?

A. Correct.

Q. Can you tell me where you obtained  
that degree, sir?

A. University of Witwatersrand.

Q. I am sorry, can you repeat that?

A. University of Witwatersrand.

Q. In South Africa?

A. In Johannesburg, yes.

Q. And was that also the university  
where you later obtained in 1965 a Master of Science  
in Organic Chemistry?

A. That is correct.

Q. Did you as well obtain your Ph.D.  
in Biochemistry from that university in 1968?

A. Yes.

Q. And you obtained, as I understand  
it, a Diploma in Clinical Chemistry in 1976 from the  
University of Toronto?

A. Right.

Q. And you have had, as I understand  
it, a varied work experience in that you have held  
various positions both in a research capacity and as







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lecturer both here and in South Africa from the  
period 1964 through to 1972?

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A. Right.

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Q. And from August 1972 to  
September of 1974, as I understand it, in looking at  
your curriculum vitae, you were employed variously  
at the University of Toronto as a Lecturer in  
Clinical Chemistry, at St. Michael's Hospital and  
the Hospital for Sick Children?

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A. Right.

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Q. During that period of time, can  
you tell me, sir, in what capacity you were employed  
by the Hospital for Sick Children. We are talking  
1972 to 1974?

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A. I was involved in the Diploma  
Program at that time which means that I was a student  
at both hospitals mentioned, St. Michael's and Sick  
Children's Hospital.

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Q. Thank you, Doctor. I take it  
at a subsequent time in June of 1975 you joined the  
staff of the Hospital for Sick Children?

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A. Yes.

Q. And you did so at that time, if  
I have it correctly, sir, as Assistant Biochemist in  
the Biochemistry Department?





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A. Right.

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Q. And that was in the Service

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Division as opposed to the Research Division of the  
Biochemistry Department?

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A. Correct.

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Q. And subsequently, as I understand

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it, you became at some point an Associate Biochemist  
in that Department?

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A. Right.

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Q. Can you tell me when that

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happened?

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A. October of 1978.

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Q. And in April of 1980 you became

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an Associate Professor with the Departments of  
Clinical Biochemistry and Pharmacology at the University  
of Toronto?

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A. Right.

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Q. And you continue today to hold

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those appointments?

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A. Yes.

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Q. I note from your curriculum

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vitae again, Dr. Soldin, that you became Director of  
what is known at the Hospital as the Therapeutic  
Drug Monitoring Program. Is that correct?

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A. Correct.

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Q. When did you become Director of that Program?

A. Actually that was mid-October of 1981. The Letter of Appointment I believe was mid-October of '81.

Q. Did that coincide, Dr. Soldin, with the introduction of the Program itself in the Hospital? Had there been a Director of that Program prior to yourself?

A. No, there had not been.

Q. You were the first Director?

A. Right.

Q. Are you today still the Director of the Therapeutic Drug Monitoring Program?

A. I am, yes.

Q. Are you still an Associate Biochemist at the Hospital?

A. I am, yes.

Q. In your capacity as an Associate Biochemist, to whom do you report?

A. To Dr. Hill, as Associate Biochemist.

Q. And in your capacity as Director of the Therapeutic Drug Monitoring Program, to whom do you report?







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A. Currently?

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Q. Currently.

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A. To Dr. Goldberg and Dr. MacLeod.

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Dr. Goldberg is Biochemist-in-Chief and Dr. MacLeod is Director of the Division of Chemical Pharmacology.

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Q. And as well you belong to a

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number of professional organizations and associations, and, to use Mr. Lamek's phrase, I do not propose to

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embarrass you by going through those at length, but

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they are set out in your curriculum vitae. Is that

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correct?

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A. Yes.

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Q. As well, you have either authored

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or co-authored a number of articles in the area of Clinical Biochemistry?

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A. Right.

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MS. CRONK: Could I ask that the

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Curriculum Vitae be marked as the next exhibit, sir?

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THE COMMISSIONER: Exhibit 23.

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--- EXHIBIT NO. 23: Curriculum Vitae of  
Dr. Steven John Soldin.

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MS. CRONK: Q. I ask you, Dr. Soldin,

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whether your appointment as Director of the Therapeutic

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Drug Monitoring Program coincided with the introduction

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of that Program in the Hospital?

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Can you tell me, prior to October of

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1981 was there a formalized Therapeutic Drug Monitoring Program in the Hospital?

A. There was no formalized Therapeutic Drug Monitoring Program. Drug monitoring did occur but it was scattered throughout the Hospital.

If you go back in the history of the drug monitoring at Sick Childrens I believe I am correct in saying that the first drug that the Chemistry Division was responsible for measuring was in fact digoxin, and that occurred in 1974.

Prior to that, no drugs were assayed within the Service Division of the Chemistry Department.

MR. SCOTT: Dr. Soldin, it might be helpful if you could try and give Ms. Cronk a little attention, but the Commissioner is entitled to a little too, so if you could just face around --

THE COMMISSIONER: Could you move the thing down a bit. I think Mr. Scott's suggestion may be helpful. We may have to do some geographical changes because it is natural to.

MS. CRONK: Would it be easier, sir, if I move to the other lectern?

MR. SCOTT: The "people's lectern".

MS. CRONK: The people's lectern.





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THE COMMISSIONER: It might be. Is it just as convenient?

MS. CRONK: I have no difficulty with that at all.

THE COMMISSIONER: It depends - if you have a tremendous number of documents it is easier to get close to the witness but there is a tendency, and it is the polite thing to do, to speak to the person who is speaking to you, but sometimes other people are listening.

THE WITNESS: I apologize for that.

THE COMMISSIONER: No, no, no, it is not your fault. It is our fault.

MS. CRONK: Thank you, Mr. Commissioner. I am sorry I did not perceive that earlier.

Q. Dr. Soldin, returning to the question of when the program was formally introduced to the Hospital, do I take it then - you indicated that the drug monitoring did take place but it was scattered at the Hospital.

Do I take you in that sense to mean that there were physical areas within the Hospital where drug monitoring was carried out?

A. Right. Prior to 1974, no drug monitoring occurred in Chemistry. In 1974 I believe







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the digoxin assay was introduced in the Chemistry Division, the Service Division of the Biochemistry Department. Some monitoring occurred of anticonvulsant drugs in a research laboratory that was run by Dr. Lowden at this time. So that was again a different laboratory.

I cannot tell you when the Department of Microbiology became involved in the measurement of aminoglycosides. I do not have that information.

Q. Can you help us, Dr. Soldin, with what the purpose of the Therapeutic Drug Monitoring Program is as it has now come to be in the Hospital?

A. The overall purpose has to be in an attempt to optimize patient care.

Perhaps at this point I could spend a few minutes discussing the rationale for therapeutic drug monitoring.

Q. I understand in that regard, Dr. Soldin, that you brought with you a number of slides which you think might graphically explain to the Commissioner and others present what the purpose of the Program is. If this is an opportune time, perhaps you could show them to us.

A. Thank you.





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Q. Can you tell us what that slide is intended to depict, Dr. Soldin?

A. As Dr. Ellis has mentioned, there are thousands of drugs in the pharmacopeia and yet there are only a few drugs which therapeutic drug monitoring is used for in the improvement of patient care. You can ask yourself why is this so? Basically the drugs have to meet certain clear criteria before therapeutic drug monitoring becomes a useful practice.

This slide is taken from some work which was carried out at the Massachusetts General Hospital several years ago and they were looking at adult patients, 200 patients of epilepsy and all of these patients were being treated with phenytoin and all of them were receiving the same dose of drug, namely 300 milligrams per day.





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The samples were drawn for analysis at the appropriate time for sampling, which is just prior to the next dose, and the serum concentration of this drug phenytoin.. was then measured in these 200 patients.

As you can see, a large -- we get quite a scattered range of serum concentrations.

Now, the therapeutic range for this particular drug is usually thought to be between 10 and 20 mg per litre and, in fact, only something of the order of 28 per cent of the results fell within 10 and 20 milligrams per litre; that is, there were fully some 60 per cent of the results that fell below what is the accepted therapeutic range for phenytoin in the treatment of seizures.

Q. If I can interrupt you, Dr. Soldin, was the same amount of drug administered to each of the 200 patients?

A. Right, 300 mg of phenytoin was administered to each of these patients.

Only some 28 per cent had concentrations within the therapeutic range and some 12 per cent had concentrations in the toxic range.

What this study clearly identified was that, if you give a certain dose of this drug







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to patients, you cannot predict the serum concentration which will arise, and only some 28 per cent - which is a rather small percentage - had concentrations within what is regarded as the acceptable therapeutic range.

Q. If I could stop you there, Dr. Soldin. Does the amount of concentration of serum as a result of the administration of the drug depend on the clinical condition of the patient?

A. I'm sorry, could you rephrase that for me?

Q. Yes.

MR. SCOTT: While it is being rephrased, I don't want to be the stage director, but it might be a little easier if you stood over on the other side of the screen. We really must start paying a little attention to the Commissioner here.

THE COMMISSIONER: Well, don't spoil him! Perhaps you might back up here and use this other one.

MS. CRONK: Thank you, Mr. Scott.

If you pick that up too far, Mr. Scott, we're in a lot of trouble!

MR. SCOTT: If we could get this around this table leg, we're in business.





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THE COMMISSIONER: While we are considering all these stage directions, Doctor, you said 12 per cent were in the toxic range; do I have that correct?

THE WITNESS: Yes, approximately.

THE COMMISSIONER: It seems to me that none of them were in the toxic range but 10 to 20 was therapeutic. Maybe I don't understand that.

THE WITNESS: Well, you can see that many of the patients had concentrations greater than 20; in fact, approximately 12 per cent.

THE COMMISSIONER: All right. I see.

THE WITNESS: Had concentrations greater than 20, which very often is associated with toxicity for this particular drug.

THE COMMISSIONER: The concentrations, then, I take it, are at the bottom? Is that the figure?

THE WITNESS: Correct. Concentrations are at the bottom.

THE COMMISSIONER: I see. Well, on the side, you have --

THE WITNESS: That's just percentage of patients having particular concentrations.





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MS. CRONK: Q. Do I take it, then --  
I'm sorry, Mr. Commissioner.

THE COMMISSIONER: No, no, I'm just --  
my mind is working, but slowly.

So, some of them were up, I take it,  
if I can read this properly, up around 60; were they?  
Concentrations of 60 nanograms?

THE WITNESS: Well, between 50 and  
52.

THE COMMISSIONER: 55?

THE WITNESS: Nobody was over 55.

THE COMMISSIONER: All right.

MS. CRONK: Q. Do I take it then,  
Dr. Soldin, that one of the purposes of this slide  
is to illustrate that, even when a fixed amount of  
a drug is administered to a set number of patients,  
the concentration of the drug in any individual  
patient, that may differ from the other patients in  
the study group?

A. That is correct. In fact, that  
is one of the prerequisites for drug monitoring. If  
one can predict the concentration in serum very  
accurately with a drug dose, then there is no reason  
to measure the concentration.

Q. All right. And is that







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concentration variability from patient to patient  
equally true, in your experience, with the drug  
dioxigin?

A. That's correct.

Q. All right. Thank you.

Can you tell me, Dr. Soldin, was  
there another slide that you wish to refer to?

THE COMMISSIONER: This drug, what  
was that drug called that we have for epilepsy? What  
was the name of the drug?

THE WITNESS: That drug is phenytoin.  
The older name is diphenylhydantoin. It is a drug  
used for the treatment of epilepsy, seizures and  
so on.

Essentially, this slide shows the  
reasons why, for some of these drugs, one cannot  
predict the serum concentration for a specific  
dosage prescribed. The variables are in the top  
half of the slide. The first is patient compliance.  
The patient may or may not take the drug as required  
or requested by the physician.

Now, patient non-compliance, for  
example, has been shown to give rise to about a  
third of the results which fall below the therapeutic  
range, if one reads the literature in this area.





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If we assume that the appropriate dosage is taken, there are still variables in absorption. For example, the absorption of the drug may vary from one individual to the next. It may vary, depending on whether the drug is taken together with meals or not, depending on whether the drug is taken together with other medications or not. There are variables in the distribution of the drug because people have different sizes and shapes and there are variables in the biotransformation or the metabolism of the drug.

Many drugs are metabolized by what is known as the hepatic microsomal enzyme system, and that system can be enhanced, or the activity of that enzyme system can be enhanced, by a number of factors, including drugs such as phenobarbital or diet, the eating of charbroiled meat, for example, or the smoking of cigarettes.

So, small factors can influence the rate at which the drugs are metabolized or converted into byproducts.

Then we have possible variables in the excretion of the drugs.

Because of all these variables, it is impossible, for some drugs, to predict the serum





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concentration for a given dosage that is prescribed.

Now, the excretion part is quite important when it comes to digoxin and especially when we talk about interferences from other drugs, interferences in the way digoxin is handled by the body by other drugs, and it has already been mentioned by several people in this courtroom that quinidine is one of the drugs that alters the clearance of digoxin renally. And other drugs that one can think of in this regard are verapamil or amiodarone or indomethacin, spironolactone as well.

So that, if any patients are placed on any of these other drugs, it could interfere with the handling by the body of digoxin, and it could alter the concentration of digoxin in the body and, clearly, at that point, it would be very important to measure the concentration and follow the patient closely so that appropriate adjustment in the dosage regimen can be made when required.

MS. CRONK: Q. If I could stop you there, Dr. Soldin, for a moment.

You have spoken specifically about the importance of the excretion factor with respect to the drug digoxin. Are all the other factors that you have described as being part of the reason for







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variability in concentration equally applicable to digoxin as they are to other drugs? Are they as relevant to digoxin as they are to others?

A. Well, I think the excretion route is particularly relevant.

Q. Fine. Thank you.

Is there anything further on this slide that you wish to draw our attention to?

A. The next requirement for a therapeutic drug monitoring that a drug has to meet is that there should be a good correlation between the serum and the pharmacological effect.

The next slide perhaps shows --

THE COMMISSIONER: I take it these slides are going to be available again in some sort of documentary form?

MS. CRONK: I have discussed with Dr. Soldin reproducing copies of those various slides.

My understanding is that you have that available?

THE WITNESS: I have copies here, yes.

THE COMMISSIONER: Yes. All right.

Thank you.

MS. CRONK: Fine.

A. There should be a relationship





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between the serum concentration and the pharmacological effect. In other words, there should be a concentration at which the drug is probably sub-therapeutic, another concentration at which it is probably therapeutic and, finally, a concentration at which it is potentially or possibly toxic.

This slide deals with theophylline, which is an important drug used in the treatment of asthma, and shows that these conditions are, in fact, met for theophylline; that between 0 and 10 mg per litre, theophylline is usually sub-therapeutic; it is usually effective and therapeutic between 10 and 20 mg per litre and, at concentrations greater than 20, it becomes toxic.

Now, for digoxin, the same is true, except we are not talking about 0 to 10 for sub-therapeutic, but we're talking about 0 to .8 nanograms per millilitre; for therapeutic range, we're talking about from 0.8 to 2.0 nanograms per millilitre. Potential toxicity can occur at concentrations usually above 2.0 nanograms per millilitre.

Q. Could I stop you for a moment, Dr. Soldin.

Are the ranges that you have just given us applicable to adults or infants?





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A. They are applicable to both,  
in my opinion.

Q. All right.

A. Now, the ranges are not hard  
and fast rules. What we are saying is that the  
majority of patients who have concentrations below  
0.8 nanograms per millilitre will have ineffective con-  
centrations of digoxin, but in some the clinical  
effects may be adequate even though the concentration  
is less than the so-called therapeutic range.

Q. And is the adequacy of that  
dosage a determination that the physician would  
make once the level was known?

A. That's a clinical decision.

Q. Thank you.

A. The same is true for the  
higher range. At concentrations above 2, you may  
not necessarily have toxicity, but you may, and  
that, again, is a clinical decision.

Q. All right.

We have heard evidence as well, Dr.  
Soldin - and perhaps I should ask you this: Were  
you present in the courtroom throughout the evidence  
of Dr. Ellis?

A. I was, yes.







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Q. All right.

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We have heard evidence with respect to the reference values for digoxin that are set out in the Residents' Handbook in Pediatrics at the Hospital, and mention is made in respect of those reference values found at page 365, and I am referring to Exhibit 16, to an overlap area.

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In the values that you have just given to us, is there, in your judgment, an overlap area between the probably therapeutic range and the potentially toxic range?

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A. Yes, there is an overlap area and, usually, this is somewhere between 2 and 3 nanograms per millilitre.

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Q. I'm sorry, Dr. Soldin, the overlap area is somewhere between 2 and 3 nanograms per millilitre?

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A. Between the therapeutic and the toxic range, usually, yes.

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Q. In respect to the drug monitoring program of which you are the Director, what are your responsibilities primarily in that position?

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A. Well, broadly, it is to optimize the program. So, my responsibilities involve trying to ensure that we get the right sample at the





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right time because interpretation of results is impossible very often unless that occurs.

Q. Does that apply to the monitoring of all drugs prescribed and administered to patients within the Hospital?

A. It applies especially to the monitoring of drugs which have a very short half-life; that is, they clear quickly from the body. So, the time of sampling relative to the time of dose is essential when the drugs have a short half-life.





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THE COMMISSIONER: A short --- ?

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THE WITNESS: Half life.

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Q. A half life?

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A. A half life. That is the time

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it takes for the concentration to drop to 50 per cent  
of its original concentration.

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Q. Dr. Soldin, since the introduc-

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tion in a formal way of the program in October of  
1981, are assays conducted for digoxin run under

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the auspices of the Therapeutic Drug Monitoring

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Program?

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A. Yes, they are.

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Q. Where is the program headquartered

14

in the Hospital in a physical sense. Are there

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particular facilities in the Hospital from which you  
perform your duties as Director of the Therapeutic

16

Drug Monitoring Program?

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A. Right.

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Q. Where are they located, sir?

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A. It is on the third floor,

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Room 3415.

21

Q. Is that the main biochemistry

22

laboratory in the Hospital?

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A. It is part of the biochemistry

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laboratories, yes.

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Q. Is it the laboratory from which  
Dr. Ellis works?

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A. No, he is across the corridor.

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Q. Dr. Soldin, during the period  
July 1980 to March 1981, I would ask you to direct  
your mind to that time frame, was the laboratory in  
which you then worked involved in the testing of  
digoxin levels in the Hospital, during the period  
July 1980 to March 1981?

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A. No, it wasn't.

11

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Q. Were you yourself involved in  
digoxin assays at that time?

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A. Not usually, no. I was involved  
on the one occasion when I was the clinical chemist  
on call, and so I had some involvement in one, in  
a couple of the cases.

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Q. When you say the one case and  
the cases, and more evidence will be heard particularly  
about samples that were or were not taken on the  
children that this Commission is particularly inter-  
ested in. Do I take it that you were the biochemist  
on call, first of all, would that refer to the  
evening shift, or the weekends, or to both?

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A. To both.

Q. And when you were on call you





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might or might not be called in to do a digoxin assay on a particular sample, is that correct?

A. To do or supervise digoxin, right.

Q. Now subsequent to March of 1981, dealing with the time frame following the Inquiry period, did your laboratory become involved under your direction in conducting digoxin assays in the Hospital?

A. Yes, they did.

Q. When did that commence, sir?

A. In July of 1981.

Q. From that point on was your laboratory responsible for all or part of the digoxin assays that were being conducted?

A. At that time it was responsible for all the digoxin assays that were being conducted at the Hospital.

Q. And is that the situation today?

A. Not at the present time, no.

Q. When - let me understand this then, during the period of July 1980 to March of 1981 your laboratory was not involved in conducting digoxin assays but you yourself might have been called in on occasion if you were on call to conduct





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or supervise such an assay, is that correct?

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A. Right.

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Q. And then starting in July of

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1981 your laboratory took responsibility for all

6

digoxin assays in the Hospital?

7

A. Correct.

8

Q. When did that change?

9

A. That changed in the fall, I think October or November of 1982.

10

Q. And what happened at that time?

11

A. At that time there was a great deal of clinical pressure on the Therapeutic Drug Monitoring Program to offer the analysis of methexate which is a drug used for the treatment of cancer. In order to accommodate this particular assay we needed more time, or staff. Staff wasn't available and Dr. Ellis' lab was able to undertake, to provide the measurement of digoxin during the week, that is Monday to Friday.

19

Q. And what happened on weekends?

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A. On weekends my staff provided the analysis of digoxin. Also they provided the stat analysis, that is if an urgent request occurred during the week that urgent request was usually done by my staff.

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Q. So if I understand it correctly,  
Dr. Soldin, after November 1982, Dr. Ellis' laboratory  
again resumed the responsibility for conducting  
digoxin assays Monday to Friday, during the week,  
save for emergency or stat assay requests which would  
be conducted by your laboratory?

A. And save for weekends, yes.

Q. Save for weekends?

A. Yes.

Q. Is that the situation as we  
sit here today?

A. Yes.

Q. What methodology for the  
conducting of digoxin assays are you currently using  
in your laboratory, Dr. Soldin?

A. We are using both radioimmunoassay  
and fluorescence polarization immunoassay.

THE COMMISSIONER: I'm sorry, could  
you repeat that?

MS. CRONK: Q. I'm sorry, Doctor,  
could you repeat the second?

A. Fluorescence polarization  
immunoassay.

Q. We have heard some reference  
in this Court Room, Dr. Soldin, to a methodology





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for the conducting of digoxin assays known as the  
TDX, is that the fluorescence polarization immunoassay?

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A. That is correct.

5

Q. What do the initials TDX stand  
for?

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A. TD probably stands for  
therapeutic drug but X I have no idea.

8

9

Q. Am I correct that that is  
merely the logo on the equipment supplied by the  
manufacturer?

10

11

A. It is a trade name.

12

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Q. And the methodology is in fact  
as I have referred to and you have just mentioned  
it fluorescence polarization immunoassay?

14

15

A. Correct.

16

17

Q. For the sake of convenience  
can I refer to that as the FPIA, if I can remember  
it that way, Dr. Soldin?

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A. Yes.

19

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Q. When did the hospital begin  
to use that method for digoxin assay testing?

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A. The history of the fluorescence  
polarization immunoassay, at least my history with  
it, dates back perhaps four years when Abbott who  
market this, approached our laboratory and myself





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four years ago to evaluate a prototype of this machine. This was done only for theophylline, the measurement of theophylline at the time. Then approximately a year ago we acquired an instrument which they were then marketing at this point to evaluate and we did an evaluation on that instrument over a period of one month. We then, in March of 1983, acquired an instrument at the Hospital for Sick Children.

THE COMMISSIONER: Is this a different instrument or the same instrument?

THE WITNESS: Essentially the same one that we had evaluated. Well, it is not the identical machine that we evaluated.

MS. CRONK: Q. The same system?

A. The same system.

Q. So I can be clear about this, Dr. Soldin, was the machine or the equipment that you evaluated last year for 1982 supplied to you by the Abbott Company that you referred to a few moments ago?

A. Correct.

Q. Did you evaluate it for the purposes of digoxin assays at that time?

A. Yes, I did.







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Q. And when you say you obtained an instrument in March of this year, was the equipment that you obtained again supplied to you by the Abbott Company?

A. Correct.

Q. And that is the FPIA technique or methodology, it is the hardware to permit tests on that equipment to be conducted?

A. Right.

Q. Was that obtained for the purposes of conducting digoxin assays, or assays for other drugs, or both?

A. Both.

Q. Since March of this year when you acquired that instrument, have you been conducting digoxin assays on the FPIA?

A. Yes, we have. We again had a period of evaluation which lasted again approximately one month, and then we started using the instrument. At the present time it is only being used for digoxin for stats requests.

Q. By stat do I take it you mean emergency?

A. Yes, right. So that is the present situation. However, we have had several





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2 meetings at the hospital evaluating the results that  
3 we have obtained on this equipment and I think  
4 within the two to three weeks we will move all the  
5 digoxin assays to the fluorescence polarization  
6 immunoassay procedure.

7 Q. And discontinue at that time  
8 conducting those particular kinds of assays on the  
9 RIA?

10 A. Correct.

11 THE COMMISSIONER: This is a totally  
12 independent procedure, is it not; that is, the FPIA  
13 procedure is all you do when you do it, is that  
14 right?

15 THE WITNESS: That is correct.

16 MS. CRONK: Q. Now, as I understand  
17 it, Dr. Soldin, from what you have told us in July  
18 of 1981, backing up, your laboratory became involved  
19 in running the digoxin assays and on various levels  
20 of involvement have been continuing to do that to  
21 date. So I take it you have had some experience in  
22 using the RIA methodology for digoxin assays in  
23 addition to the FPIA methodology.

24 A. Right.

25 Q. Is that correct?

A. Right.





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Q. When you say, Dr. Soldin, that you anticipate that within the next two to three weeks all digoxin assays in the hospital will be run on the FPIA method, is that a matter that is now actively under consideration, or has a determination been made to switch fully to FPIA system?

A. That has been actively considered and we had several meetings. We have spoken to the staff people involved, that is the head of Cardiology, the Neonatal group, and various other medical directors, et cetera. The decision has been made to switch, yes.

Q. As I understand it, Dr. Soldin, the FPIA technique is similar in basic concept to the radioimmunoassay technique, and you can correct me if my understanding is wrong. I take it that essentially the basic principle that is involved with the FPIA is once again a competition between a particular kind of molecule that has been treated in a particular way with a patient sample, a competition between those two for a binding site on an antibody that is used in the process.

A. That is right.

Q. Is that a fair statement of the basic principles?







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A. Right.

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Q. And I take it with the FPIA

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method you do not use radioactive digoxin, or a

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component treated with iodine 125 for radioactive

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purposes, but rather you use a substance that has

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been labelled with fluorescein, is that correct?

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A. That is correct.

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Q. I would like to review very

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briefly with the component parts of the FPIA test,

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Dr. Soldin. Am I correct that standards are

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involved in the use of this methodology as well?

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A. Yes.

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Q. How many standards are required?

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A. There is a zero standard and  
five others, so there is six altogether, five plus  
a zero.

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THE COMMISSIONER: I am sorry, there

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is a which standard?

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THE WITNESS: There is a zero.

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THE COMMISSIONER: A zero standard?

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THE WITNESS: Yes, zero, 0.5,

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1, 2, 3 and 5 nanograms per millilitre.

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MS. CRONK: Q. And are those

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standards manufactured or produced for you in the

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hospital or do you obtain those commercially?

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A. They are obtained from Abbott.

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Q. From Abbott Company?

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A. Yes.

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Q. And indeed, perhaps with

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respect to each of the components of the test that

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we will be discussing, are any of the components

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purchased or supplied to you from other than the

9

Abbott Company?

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A. Not for the conducting of

the actual assay, they are all purchased from Abbott.

11

Our quality control material is not.

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Q. Well, I will come back to the

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control samples in a moment, Dr. Soldin. Dealing

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still with the standards what purpose do they

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serve in conducting an FPIA assay?

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A. The same purpose that they

serve in conducting an RIA assay, which is to

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obtain the calibration graph so that the patient

18

samples can be read off this graph.

19

Q. So I take it that you use those

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standards to calibrate the machine at the outset of

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the assay, is that correct?

22

A. Right.

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Q. How often, using the FPIA

method is it necessary to calibrate the equipment

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before running an assay?

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A. Well, at this time we are calibrating once a week and that is proving very adequate. It may be that one only has to calibrate once a month, but that study we haven't yet performed. Certainly the calibration period unlike radioimmunoassay only has to be run at the most weekly.

Q. And I take it, because we have heard evidence from Dr. Ellis, that with the RIA method it is required that the standards be used to calibrate the machine before each and every assay, do you agree with that?

A. Right.

Q. So that with the FPIA there is a marked distinction in terms of the requirement for calibration of the machine?

A. Right.

Q. And I take it a concomitant time saving involved with that?

A. Time and funding ultimately, yes.

Q. Yes, I appreciate that as well, Dr. Soldin. You mentioned quality controls. It is my understanding that like the RIA methodology, once again, control samples are required and used to







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conduct an FPIA test, is that correct?

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A. Right.

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Q. How many control samples are

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used?

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A. Three.

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Q. And what are the concentrations

of those control samples?

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A. I will have to look them up.

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MS. CRONK: You will notice, sir,

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that Mr. Scott has arranged that I am sufficiently

11

far back from the flip chart there that I can't

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possibly do damage with it, with a felt pen in my

13

hand again.

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THE COMMISSIONER: I think he under-

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estimates you, I'm sure you can manage it if you

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are determined.

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THE WITNESS: 0.6, 3.1 and 1.5

nanograms.

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THE COMMISSIONER: I'm sorry, can

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I have those again?

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THE WITNESS: 0.6, 1.5 and 3.1

nanograms per millilitre.

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MS. CRONK: Q. When I referred to

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concentrations in that context, am I correct that

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that refers to a fixed amount of digoxin that is

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introduced to each of the control samples?

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A. That is right.





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Q. And where do you obtain the control samples that you use for the FPIA assay?

A. From Hyland.

Q. I'm sorry?

A. From Hyland Laboratories.

Q. Is that the exception that you referred to a moment ago, all the other required components for the test being purchased or obtained from Abbott, with the exception of the control samples?

A. Right.

Q. You indicated to me a few moments ago that the FPIA methodology does not entail the use of radioactive digoxin but, rather, digoxen that has been labelled with fluorescein; is that correct?

A. Correct.

Q. And that is the next part of the assay that is required before we come to the antibody, and that is fluorescein labelled digoxin?

A. Right.

Q. Where do you obtain that, for the purposes of conducting an assay?

A. From Abbott.

Q. And like the RIA methodology,





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there is a set or fixed amount of fluorescein labelled added to both the standards that you use on the assay and the control sample?

A. Correct.

Q. Are the standards and the control samples run through the assay at the same time that the patient sample is?

A. The standards, as I have explained, are run only once a week.

Q. I'm sorry, all right.

What about control samples?

A. The control and patient's are run with every batch.

Q. And the next component part is, obviously, the patient sample itself and the sample of interest in respect of which the assay is, in fact, being run?

A. Right.

Q. Is there a particular kind of sample that is used on the FPIA as compared with the RIA? For example, do you run FPIA digoxin assays on whole blood samples?

A. No, serum or plasma.

Q. Is the FPIA, in fact, designed to accommodate testing on tissue samples?







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A. Not to my knowledge.

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Q. Have you attempted to use it

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for that purpose since its acquisition in the  
Hospital?

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A. No.

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Q. The next component, and again

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correct me if I am wrong in my understanding, Dr.

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Soldin, the next component of the assay is, in fact,

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the antibody.

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Do I take it that that, as well, is

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supplied as part of the kit that you obtain from

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the Abbott company?

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A. Right.

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Q. Is the purpose of that anti-

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body in this assay similar to the purpose of the  
antibody in the RIA assay?

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A. Yes.

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Q. By that, would I be correct

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in taking it that its purpose -- first of all, that

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it has an avidity or attraction for both digoxin

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and for fluorescein labelled digoxin?

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A. Right.

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Q. And the purpose of the assay,

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or the basic principle involved, is that the

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fluorescein labelled digoxin will compete with the

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patient sample digoxin for a binding site on the antibody?

A. Right.

Q. Can you tell me, Dr. Soldin, in this particular assay, is there any need after the interaction of the fluorescein labelled digoxin and the patient sample digoxin with the antibody has taken place, after that part of the step has been completed, is there any need to separate the amount of bound digoxin from unbound digoxin?

A. No.

Q. Can you tell me why that is so?

A. Because, here, we are measuring a change in polarization which does not require such a separation.

Q. Dealing with the change in polarization, so I might understand that, as I understand, the principle of the fluorescein labelled digoxin is such that a polarized light is shone, by virtue of the equipment, through the component or the mixture that you have, which includes both the fluorescein labelled digoxin and the patient sample digoxin together with the antibody; is that correct?

A. Correct.





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Q. As I understand it, the degree to which the fluorescein labelled digoxin has become bound to the antibody is reflected in the kind of light or the plane of light that is emitted at the other end of the process; is that correct?

A. Yes.

Q. How do you know whether or not the fluorescein labelled digoxin has effectively won the competition and more of it has bound itself to the antibody than the patient sample digoxin?

A. By measuring the light intensity at the other end.

Q. What do you expect to see in terms of intensity if the fluorescein labelled digoxin has bound itself to the antibody in a higher proportion or volume than the patient sample?

A. You will get a strong signal if the fluorescein labelled digoxin has linked up with the antibody.

Q. And conversely, if a weak signal results in the process, do I correctly take that to mean that a greater proportion of the patient sample digoxin has bound itself to the antibody than has the fluorescein labelled digoxin?

A. Right.







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Q. So the basic principle then is, if I understand it correctly, the lower the light that is emitted at the end of the process on a polarized plane, the greater is the amount of the patient digoxin that has become bound?

A. Correct.

Q. And conversely, the higher amount of light that you can detect at the end of the process on a polarized plane means that a greater amount of fluorescein labelled digoxin has become bound and, correspondingly, a lower amount of patient digoxin has become bound?

A. Right.

Q. How is that light measured? Is that a function of the equipment itself, doctor, or are we talking about something akin to a gamma counter that tells you what is there?

A. It is measured by the usual way of measuring light intensity, which is by converting the light signal into an electrical signal and employing a photomultiplier tube.

Q. Is that done electronically?

A. It is done electronically.

Q. After that has been done and you have been able to identify, by the electrical





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reading, the amount of polarized light that has resulted from the process, how do you then make the step of knowing how much patient digoxin is, in fact, bound and present in the sample?

A. When you read the result of the calibration curve.

Q. And are we then again involved in a plotting process as described by Dr. Ellis?

A. Yes.

Q. Would I be correct then, Dr. Soldin, that, at the end of an FPIA assay, you know how much fluorescein labelled digoxin is contained in the standards and you can plot the curve of that because you know the fixed amount that was introduced into the standards at the outset?

A. Correct.

Q. And you can then compare the values that you would expect to see, given the known amount of digoxin in those standards; you can then compare that with the reading that you have obtained electronically as to the amount of fluorescein labelled digoxin in the patient sample, the end compound?

A. Right.

Q. Am I correct as well, Dr.





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Soldin, that whatever else is in the patient sample, there is another similarity between the RIA and the FPIA method, and that is, only substances that are digoxin, digoxin byproducts or that react like digoxin in respect of the antibody, will be involved in the binding process that takes place in the FPIA assay?

A. Correct.

Q. Now, can you tell us briefly, Dr. Soldin, in your view, what advantages there are, if any, to the FPIA system versus the RIA system?

A. I have written up a list of advantages for the Hospital and I would be prepared to make it available to this hearing if you wish.

Q. We would be glad to see that, doctor.

A. Some of the obvious ones are that fluorescence polarization immunoassay as conducted on the Abbott analyzer enables a digoxin measurement in a very short time interval.

Q. How long would it take, doctor, to do an assay for digoxin on the FPIA?

A. Approximately twelve minutes for a single result and approximately 20 minutes for 20 results.







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Q. I'm sorry, for 20 results?

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A. Right.

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Q. And that is compared to what

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time period, in your view, based on your experience,  
on the RIA?

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A. That is compared to two to

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three hours on the RIA system.

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Q. Is that, on the RIA system,

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for one sample or for 20 or for something in between?

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A. The difference for one and

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20 is not that great; so two hours would be the  
minimum for one, and a batch of 20 may take three  
hours.

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Q. Are there any other advantages

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or distinctions between the FPIA methodology and  
the RIA methodology?

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A. The FPIA methodology is

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extremely simple, technically, so that, apart from  
being rapid, it is extremely simple, so that less  
technical time is involved.

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Q. And by that do you mean

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personnel time?

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A. Personnel time.

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Q. Less time for the technologists

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who work in the laboratory?

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A. Right.

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Q. Any other advantages?

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A. There are other possible ad-

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vantages. The FPIA system precipitates the proteins

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prior to analysis of the sample and, should any

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compound be attached to the proteins that would

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interfere with the analysis, that would thereby

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remove such a compound.

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Q. My understanding of the use

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of the word "precipitates" in that context, Dr.

Soldin, is that it separates.

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A. Separates.

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Q. When you say that there is a

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protein precipitator, do I take it that the pro-

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teins are separated from the sample that you are

testing?

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A. The proteins in the sample

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are removed prior to analysis.

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Q. Is that right at the beginning

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of the assay?

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A. Correct.

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Q. How is that accomplished?

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A. By the addition of a precipi-

tating agent, trichloroacetic acid.

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Q. And is there a similar step

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in the RIA process that you use?

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A. No.

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Q. Is it a recommendation of the Abbott company or is it part of the materials that they provide to users that that precipitating agent be used for protein separation at the beginning of the assay?

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A. That is correct.

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THE COMMISSIONER: What is the advantage of that? What is the purpose?

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THE WITNESS: It serves several purposes. One of the advantages that I was alluding to is that it is conceivable, although perhaps not proven, that a compound may be attached to a protein or be part of a protein that might react with the antibody to digoxin. Therefore, if you can remove the proteins, you can eliminate that possible source of interference.

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THE COMMISSIONER: I just wondered, it is not proven, but have you compared the results from the FPIA and the RIA?

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THE WITNESS: We certainly did. We would never change a technique from --

THE COMMISSIONER: What I meant was, has there been a difference? Have you found --







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THE WITNESS: Well --

THE COMMISSIONER: I'm getting ahead  
of you probably.

THE WITNESS: You are getting ahead.  
Let me give you an answer on that.

We have compared samples from patients  
that are below the therapeutic range and going up  
to approximately 5 nanograms per ml; that is, the  
routine run-of-the-mill type samples that we might  
be getting at the Hospital, and when we do such a  
comparison, the results are extremely comparable  
between the two techniques. So that, for clinical  
purposes, they seem to be very comparable.

However, we have also done some  
measurements on samples obtained on patients that  
are not on digoxin and that fall in the neonatal  
period; that is, under two months of age, and the  
last group that we have done comparisons on is on  
autopsy samples.





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MS. CRONK: It is my intention,

Mr. Commissioner, if I could interrupt at this stage,  
to deal with some of those samples in a few minutes,  
if I could ask your indulgence.

THE COMMISSIONER: Yes, all right,  
I'm sorry.

MS. CRONK: No, that's quite all right,  
that's quite all right.

THE COMMISSIONER: Yes, go ahead.

MS. CRONK: Q. Dr. Soldin, turning to  
the element of speed that you described and the  
time that's required to do an FPIA assay, and you  
indicated 10 minutes for one sample. Is it 10  
minutes including the protein separation process, or  
is that time over and above?

A. I think I said 12 minutes.

Q. I'm sorry?

A. Yes, it includes the in-time  
procedure.

Q. All right. How do you know,  
Dr. Soldin, if the equipment itself is functioning  
properly at the end of an assay and there's been no  
malfunction of the equipment. Can you protect against  
that in procedures in your laboratory?

A. That's the function of the





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quality control samples which are run with every single batch of patient samples. So that provided we get results for the quality control samples that are acceptable, and I use that word in inverted commas, then we would report the results, but if the quality control samples were unacceptable, then there would be something wrong with the analytical procedure and the results would not be reported, we would have to find out what was wrong.

Q. And indeed, as I understand it, one of the primary functions of running the assay on the control samples at the same time that you're running it on the patient sample is to determine whether or not the amount of fluorescein labelled digoxin that you would expect to be in the control samples, because it's been put in there and you know the amount of it, is in fact reflected at the end of the assay so that you know that the assay is in fact recording correctly, or close to correctly, the amount that was actually in the quality control samples?

A. Yes, we're interested in the amount of digoxin in the quality control samples. We do add fluorescein label.

Q. I'm sorry.







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A. But we're interested in the amount of digoxin.

Q. The same principle is at work with respect to the digoxin in that a known amount of digoxin has been added to the control samples and you can judge at the end of the assay whether the reading corresponds, in your judgment, as being close enough or, indeed, precisely on the amount that you know in fact is in the control samples?

A. Right.

Q. Is that correct?

A. Yes.

Q. And that permits you to assess whether technically the equipment is functioning properly?

A. Correct.

Q. Thank you. Can you tell me, Dr. Soldin, how many hospitals or laboratories in a clinical setting to your knowledge are currently using the FPIA method for digoxin assays, or do you know?

A. This is changing monthly. So, the latest reports we have from the American Association for Clinical Chemistry Therapeutic Drug Monitoring Program, of which we are a member, are that in May of





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this year, 39 laboratories had basically switched from RIA, radioimmunoassay to fluorescence polarization immunoassay; that is somewhat over 10 per cent of the total number of laboratories in this program in North America. There are 385 laboratories that are associated with this program in North America.

Q And of those --

A For digoxin, sorry; for digoxin.

Q And of those in the month of May, there were 39 who were using the FPIA method exclusively?

A Correct.

Q Did that include the Hospital for Sick Children?

A No.

Q All right. Are any of the participants in the numbers that you have just given us forensic laboratories?

A I wouldn't be able to tell you that.

Q All right.

Mr. Commissioner, would this be an appropriate time for a break?

THE COMMISSIONER: Yes, all right, fifteen minutes.

--- Short recess.





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--- Upon resuming:

THE COMMISSIONER: Yes, Miss Cronk.

MS. CRONK: Thank you.

Q. Dr. Soldin, just before the break, you told me about the number of laboratories who belonged to the American Association of Clinical Chemistry that were now using the FPIA method. Is that exclusively in lieu of the RIA method or is it possible that some are using them in combination as your Hospital is?

A. Right. It is possible that some are using it in combination. It is not likely but it's possible. I should mention that those are the number of laboratories performing digoxin in the American Association program, whereas, the number that perform phenytoin or another drug are totally different.

Q. I'm sorry. So, when you talk about 39 laboratories reported as at the month of May of this year, you're talking about 39 labs using the FPIA technique for digoxin assays?

A. Correct.

Q. Do you have the number for the month of June?

A. Not yet, no, but we will shortly have.







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Q Thank you. Dr. Soldin, we also heard evidence through Dr. Ellis that at some point in time the Hospital, for the purposes of the RIA digoxin assay, ceased purchasing its standards commercially and they began to be made in the Hospital itself and his evidence was, if I recall it correctly, that you were preparing standards for the RIA assay. Is that correct?

A. My laboratory was preparing it.

Q I'm sorry, your laboratory?

A. Yes.

Q When did your laboratory begin to prepare those standards for use on the RIA assay?

A. I think it was - we took over the assay in July and I think we started preparing standards in August or September.

Q Of 1981?

A. Of 1981.

Q All right. And in the preparation of these standards, do I understand it correctly that what that involves is measuring a known amount of digoxin to be introduced and used as the standards sample both to calibrate the equipment for the RIA assay and then to be run through the assay itself?

A. Right.





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Q. All right, thank you. You mentioned again, dealing with the FPIA technique, you have told us about the time saving that's involved in using that technique as opposed to the RIA technique, both because the assay itself requires less time and perhaps as a corollary of that, because it involves less technologists' time. Now, am I correct, Doctor, in terms of the functioning of the equipment itself, there's a time saving involved first because one need not calibrate the equipment as frequently as one is required to do so on the RIA?

A. Right.

Q. All right. And, secondly, you have told us that there is no separation technique required or precipitation technique to determine or separate the amount of bound digoxin from the amount of unbound digoxin and the removal of that necessity would as well be a time-saving factor. Is that correct?

A. Correct.

Q. And in addition to that, I take that to mean that there is no charcoal involvement, or there is no reagent introduced to the assay to accomplish that?

A. Correct.

Q. All right. And the third area





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in which there would be a time saving, apart from technologists' time itself, is that there is no use of a gamma counter to do an actual reading, that there is an electronic reading done automatically on the FPIA for the purposes of measuring the amount of polarized light that is evident or existent at the end of the assay, that's done automatically by the equipment?

A. Yes.

Q. And finally, am I correct that there is also a time saving involved in the FPIA technique because as the charcoal separation step is not required, there is no requirement for the samples to incubate with the addition of the charcoal. They're not required to sit on the counter and incubate for a period of time as Dr. Ellis described?

A. There is an incubation step as part of the procedure, but it is a short incubation which occurs within the machine.

Q. All right. Now, you have told us, Dr. Soldin, what in your view are some of the advantages of the FPIA technique. Are there in your view any disadvantages to that technique as opposed to the RIA methodology?

A. The sample requirement for the







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FPIA is somewhat greater as currently used. 200 microlitres of serum or plasma are the recommended volumes required.

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Q. For the FPIA?

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A. For the FPIA. We have done studies showing that results can be obtained if one employs 100 microlitres of sample specimen. So that in the rare instances where we don't get sufficient volume, we will be able to dilute the sample with drug-free plasma and obtain a result.

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Q. That's in circumstances where you were not supplied with 200 microlitres of sampling?

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A. Right, 200 microlitres of serum or plasma, not of blood.

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Q. All right, well let's deal with that. What quantity of whole blood would be required to produce, for the purpose of the assay, 200 microlitres of sera or plasma?

A. Again, as Dr. Ellis mentioned, that depends on the hematic rate in the patient for children other than young neonates, the hematic rate may be around 50 per cent. So, one would need to double cover the volume of whole blood. So, for older children half a ml. of blood would be adequate.





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For young neonates, if the hematic rate is, say, 70 per cent, one would need a better sample.

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Q. So, it would depend on the patient's age?

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A. To some extent, yes. It depends on the hematic rate, which is usually over 50 per cent in neonates and in prematures. So, it may run as high as 70 per cent, maybe even 80 per cent.

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Q. And you've told us, Dr. Soldin, that you have conducted studies on the FPIA which indicates that it is possible, although I take it it is not desirable for you to run assays on that technique with 100 microlitres of plasma or serum as opposed to the desired 200 microlitre sample?

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A. Correct.

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Q. All right. It is possible to do an assay on less than 100 microlitres of sample?

A. It is, but it depends on the concentration of digoxin in that sample. Now, I'm talking about measuring it for concentrations between 0.8 and usually 2.0 nanograms per millilitre. I wouldn't be happy with using a very much smaller sampler at the low concentration range, but if the concentration in the sample is higher, then surely one can add quite a smaller value.





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Q. And do I take it that like with the RIA, the situation is similar with the FPIA and, that is, the smaller quantity the sample provided for testing, the lower the likelihood that increasing number of dilutions can be made, the size of the sample directly relates to the number of dilutions that one can technically perform?

A. Correct.

Q. And dealing again with the FPIA, other than the size of the samples required for testing, are there any disadvantages in your view to this technique as opposed to the RIA methodology?

A. If one works out the cost per analysis and projects that over a year, the cost per analysis for a digoxin assay is marginally higher than with the FPIA method. So that it would result in an increase in our budget for the Therapeutic Drug Monitoring Program of approximately \$1,000 per year. That's about the only other drawback.

Q. Other than economic factors or increased costs caused by this method as opposed to the RIA, is there anything intrinsic to the methodology itself which, from your view as a scientist, could be considered as a disadvantage with this methodology as opposed to the RIA?







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A. Not to my knowledge, no.

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Q. I'm correct, Doctor, am I not,

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from the evidence that you have given, that a

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different antibody is used on the FPIA system than

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is used on the RIA in that the antibodies used on the  
RIA at the Hospital are obtained from Antibodies Inc.

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from California, whereas, the antibodies that are

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used in the FPIA technique are obtained as part of

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the Abbott Kit?

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A. Correct, but then again I don't

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know where Abbott gets their antibody. So, it may

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be that they get their antibody from Antibodies Inc.

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Q. Oh, I see.

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A. It may not be.

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Q. Have you made inquiries in that

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regard?

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A. I don't know. No, I haven't

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made any.

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Q. All right. Dealing with the

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FPIA technique, we've heard evidence as well as to

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what has been described as the minimum detection

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level on the RIA, and by that, at least my under-

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standing of the concept, is, as a level -- excuse me,

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as a measure, the lowest measurable level or

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concentration which can be distinguished from zero in





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any degree of scientific confidence, is there a  
minimum detection level that applies to the FPIA  
technique?

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A. There is, the same as there is  
for the RIA technique. The problem is in deciding  
what that detection level is.

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Q. Well, as you sit here today,  
as you have used that technique in your laboratory,  
what is the minimum detection level that you treat  
as the guideline?

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A. Well, at the present time, we  
employ the same lower cutoff limit as we do for the  
RIA, which is 0.5 nanograms per millilitre. The  
Abbott literature, that is the literature from Abbott  
would indicate .2 nanograms per millilitre could be  
used as the lower cutoff. At the moment, we are  
employing 0.5.

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Q. Is that being done for any  
reason other than consistency, is that a factor at all?





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A. Well, again we are getting now into the results which we have obtained on patients that are not on digoxin and then on neonates.

Q. Perhaps I will reserve that question and ask you again when we come to discuss those test results.

Aside from the - well, you told us what the standard amount of concentrations of digoxin are in the standards that are supplied from the Abbott Company for this assay. If I understood your evidence correctly the largest concentration was .5.

A. Was 5.0.

Q. I'm sorry, 5.0?

A. 5.0.

Q. All right. So the minimum detection level is not tied in then with the amount of concentrated digoxin present in the standards?

A. One could tie it in with the lowest standard employed.

Q. Right.

A. And that is sometimes practised. So that the lowest standard employed is .5 and therefore we make a decision we are not going to report anything less than .5.







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Q. And similarly, Dr. Soldin, we have heard evidence as to what has been described as the maximum measurement capacity on the RIA method, the highest level of digoxin that can be measured on one assay without the requirement of further dilution. Is there a maximum for highest level that is applicable to the FPIA assay?

A. Again it is the highest standard concentration which is 5.

Q. And if at the conclusion of an FPIA assay in respect of any particular patient sample a reading of 5 nanograms was obtained, what would you then do in your laboratory with respect to that sample?

A. If a reading greater than 5 was obtained we would dilute the sample.

Q. And there are ---

A. If there was sufficient sample left.

Q. Assuming that there was a sufficient amount of sample initially provided, or otherwise available to you by subsequent request, are there guidelines that you employ in your laboratory as to what the first level of dilution will be, or do you do several at the same time





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depending on the amount and quantity?

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A. One would do it two times,

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five times, ten times provided there is enough

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sample.

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Q. And is there any magic to

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the 5 nanograms per millilitre figure if you got

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a result on an FPIA reading of 4.6, 4.7, 4.8, would

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you in those circumstances dilute or must it be

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5 or greater?

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A. No, it should be greater than

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5, yes.

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Q. Are you able to tell us,

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Dr. Soldin, as a result of your experience both

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with the RIA technique for digoxin assays and your

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experience with FPIA technique for digoxin assays,

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which methodology in your view is more reliable for

18

the purposes of obtaining a digoxin reading?

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A. Well, that is a difficult

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question, and the answer is somewhat subjective.

21

I think both techniques will provide good results,

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adequate results for clinical purposes in the

23

majority of cases. We have heard Dr. Seccombe and

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a few others talk about instances where substance X

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might give an erroneous result, those are relatively

rare instances.





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If one looks at total work volume of digoxin, let us say we do 20 digoxin analysis on patient samples every day, not more than one or two of those 20 would be from the Neonatal Ward and only a small percentage of those might have substance X in them. So that overall I think both methods could provide reliable clinical data.

Q. Well, Dr. Soldin, can you help me with this? You have told us that as long ago as four years ago your laboratory was approached by the Abbott Company for the purposes of creating a prototype of this methodology for use with a different drug, different kind of assay, not digoxin? I am sorry, you are hesitating.

A. That is not quite right. I was approached by the Abbott Company to evaluate a prototype that already existed.

Q. Fine. All right. Do you know when the Abbott Company first introduced on the market the FPIA system for the purposes of digoxin assays?

A. I can't give you the month, you know, I think it must be 18 months ago approximately.

Q. Would I be correct then,







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Dr. Soldin, given the relatively recent introduction of this technique by the Abbott Company, compared at least to the RIA which you have told us was in use in the hospital from 1974 onwards, that there is comparatively speaking a lower volume of literature available reporting upon results obtained pursuant to the FPIA technique than there might be reporting on results obtained from the RIA technique?

A. That is correct.

Q. And that the growth of that kind of literature I assume will be of assistance to you in assessing as a matter of your own professional judgment whether or not the FPIA technique was or was not more reliable for digoxin assays than the RIA technique?

A. That is correct. We have some of our own findings as well which may give us some opinions on this matter.

Q. All right, and I will come to that in a moment. Perhaps it is a difficulty with the words reliable. Can you tell me, Dr. Soldin, based on your comparative experience with both the methodologies whether the one as opposed to the other results in more certain, or more specific digoxin assay recordings?





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A. Well, you know I think both give equivalent results. However, if you gave me a sample and said that I could only use one method for measuring that sample, for measuring the digoxin in that sample, I would choose, with my knowledge today, to measure that sample with the fluorescence polarization technique.

Q. Is that a function of anything other than the time involved?

A. I think it does, yes, apart from the time.

Q. Can you tell me what that is?

THE COMMISSIONER: I am sorry, you are asking for the time?

MS. CRONK: No, I am sorry.

THE WITNESS: It is a function other than the time.

MS. CRONK: Q. What is there in your judgment which would encourage you to use the FPIA technique other than the factor of time on any given sample?

THE COMMISSIONER: Other than the other advantages that he has told us about.

MS. CRONK: Q. To be fair, that's right, other than the other advantages.





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A. Well, we keep coming back to the preliminary data which we have on samples of patients that are not on digoxin. The only data that we have in the autopsy comparisons are both RIA and FPIA. Do you want me to go into that? If you do then those are the reasons why I would choose the FPIA technique.

Q. All right. Well ---

THE COMMISSIONER: It is more accurate, is it? The post mortem sample, is that what you are saying?

THE WITNESS: It could be, yes.

THE COMMISSIONER: That's not quite the same, is it?

THE WITNESS: Well, I am, that is as far as I will go at this point in time. If we get into the serious of results.

MS. CRONK: Q. All right. Then again, perhaps unfairly to you I put the question prematurely and I will come to the question of sampling in a moment. With respect to the antibody that is used on the FPIA technique as supplied by the Abbott Company, have you in your laboratory used the antibodies provided by the Abbott Company on the RIA technique?







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A. No, we haven't.

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Q. Is there any reason why

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technically that could not be done?

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A. It could be done.

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Q. And if that experiment were

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undertaken would I be correct that would give you

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some basis upon which to measure whether there was

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any difference in specificity between the antibodies

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currently used on the RIA and the antibodies used

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on the FPIA? Is that one might obtain?

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A. If one compared the RIA results

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with the Antibody Inc. antibody and compared the

14

results again by RIA but at this time use the Abbott

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antibody one could get an idea of the relative

specificity.

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Q. Yes, thank you. Dr. Soldin,

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we have heard evidence as well concerning a methodology

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known as the HPLC methodology that has been used for

19

digoxin assays. Do you personally have any experience

with using that methodology for digoxin assays?

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A. Not for digoxin, no.

21

Q. Similarly, Dr. Soldin, have you

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personally had any experience in using the Beckman

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Antibody either for purposes of conducting RIA

24

digoxin assays, or FPIA digoxin assays?

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I.9

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3 A. Depending what you call  
4 personally. I haven't done tests using the Beckman  
5 RIA kit myself. However, we approached Mr. Cimbura,  
6 I can't give you the date offhand, approximately two  
7 months ago and a post doctoral fellow who was working  
8 with us has had a very brief and preliminary look  
9 at the Beckman kit as used by Mr. Cimbura. He got  
10 the instructions from the Forensic Science laborator-  
11 ies, but he has carried out these tests at our  
12 Hospital.

13 Q. Was that testing conducted in  
14 accordance with what he understood to be the  
15 methodology employed by Mr. Cimbura?

16 A. That is correct, what he  
17 understood, right.

18 Q. My question perhaps was a  
19 little different, Dr. Soldin. To be fair to you, I  
20 take it not you personally, but have any others under  
21 your supervision attempted to use the Beckman Anti-  
22 body on the RIA methodology in use in the Hospital,  
23 not Mr. Cimbura's methodology, but the approach  
24 used for RIA in the Hospital?

25 A. No, we haven't.

Q. And similarly as the Beckman  
Antibody or parts, components of the Beckman kit





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been used on an experimental or research basis in the Hospital on the FPIA technique?

A. No.

Q. Can you help us, Dr. Soldin, as to what substances or drugs have been indicated by the Abbott Company to have known levels of cross-reactivity with the Abbott supplied antibody used in the FPIA methodology?

A. Yes. The company does have a hand out on this which you might want to include in the exhibits.

Q. If I can just see what you're looking at, Doctor. Doctor, are you looking at a document which you previously provided to me through your counsel entitled "Cardiac Glycoside Drug Assays - TDX Digoxin"?

A. Right.

MS. CRONK: Copies of this, Mr. Commissioner, have been supplied to other counsel.

Q. Dr. Soldin, can you help me, is this document a document provided to you by the Abbott Company in respect of the FPIA materials supplied to you by that company?

A. Yes.







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Q. And does it indicate or contain any results, or information, with respect to cross-reactivity of other substances, or known drugs with antiserum in use on the FPIA Abbott kit?

A. Yes, it does.

Q. What page is that, sir?

A. 17.4 I think it is, Table I on 17.4.

Q. And dealing with Table 1, Dr. Soldin, the column on the left entitled "Compound Added", do I correctly take it that drugs of the compounds listed in that column are all of those in respect of which, to your knowledge, the Abbott Company has tested for cross-reactivity with its antiserum?

A. To the best of my knowledge, yes.

Q. And the next column entitled "Quantity Added", and I take that to mean as is suggested by the title the amount or volume of the compound that was added to the test sample for the purposes of running the cross-reactivity assay?

A. Right.

Q. And the third column "Average Cross-Reactivity", I take that to be the result





I.12

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obtained by the Abbott Company in conducting these  
cross-reactivity assays?

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A. Right.

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Q. Can you help me, Dr. Soldin,  
besides digoxin, the average cross-reactivity is  
shown as 100 per cent, I take that to be a  
reflection of what the Abbott Company believes to be  
the degree of specificity of the antibody to digoxin?

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A. Right, it is. Is it an anti-  
body raised to digoxin.

Q. Can you - and dealing with the  
compounds listed immediately below digoxin, given  
the similarity in their names to that of digoxin,  
do I correctly take those to all be metabolites or  
by-products of digoxin itself?

A. Right.





J/DP/ak

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Q. Can you help me as to what the 205 per cent average cross-reactivity means in respect of the compound digoxigenin?

A. That means that if one had a concentration of one nanogram per millilitre of digoxigenin it would read 2.05 milligrams in nanograms per millilitre of digoxin in the assay of the average kit.

Q. Do I correctly take it as well that from these results it would appear that digoxigenin has a larger likelihood of binding to the antibody used on the Abbott kit than does digoxin itself?

A. Right.

Q. And similarly with the next compound, that would be correct, recorded at 150 per cent?

A. Correct.

Q. And with the max at 115 per cent?

A. Correct.

Q. Going down the list of compounds added, Dr. Soldin, I note in the fourth grouping of compounds that a test for cross-reactivity was run for furosemide?







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A. Right.

Q. And that the average cross-reactivity, according to the Abbott Company was .01 per cent?

A. Correct.

Q. As well, dealing with the next group of compounds, progesterone, and I hesitate again to pronounce this, but the next two compounds all reflect low average cross-reactivity percentages insofar as the Abbott Company's research is concerned?

A. Right.

THE COMMISSIONER: What is the importance or significance of the "quantity added"?

MS. CRONS: Q. Can you help us with that, Dr. Soldin?

A. It indicates the amount that was added in order to get the reading, the particular digoxin reading, so they added 10 micrograms per millilitre of spironolactone, say, and had a cross-reactivity of 0.025 per cent.

THE COMMISSIONER: Does it affect the cross-reactivity, the fact that you have added more or less?

THE WITNESS: It would change the reading, yes. If you added 100 times as much, you





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would get a bigger reading.

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THE COMMISSIONER: All right, just

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for this simple mind, though, you have added 5 nano-

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grams in this ---

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THE WITNESS: Dihydrodigoxigenin.

7

THE COMMISSIONER: Whatever it is,

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and you have got a figure of 12 per cent.

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THE WITNESS: Yes.

10

THE COMMISSIONER: If you had

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added one nanogram, would you have got a different  
figure?

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THE WITNESS: That is my interpreta-

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tion of the data, yes.

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THE COMMISSIONER: That means that

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actually the cross-reactivity then is only one-fifth  
of 12 per cent. Is that correct?

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THE WITNESS: That is my interpreta-

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tion of this data.

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THE COMMISSIONER: Is your

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interpretation the correct one, do you think?

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THE WITNESS: You would have to

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ask Abbott that.

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MS. CRONK: Q. Have you done that,

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sir? Have you raised any enquiries with the Abbott

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Company as to the meaning of the figures that

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appear on this table?

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A. No, I have not.

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THE COMMISSIONER: What is the

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relationship between an "ug", whatever an "ug" is?

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THE WITNESS: A microgram and a

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nanogram. A nanogram is 10 to the minus 9th of

8

a gram and a microgram is 10 to the minus 6th of a  
gram.

9

THE COMMISSIONER: And the "ug"

10

stands for what, please?

11

THE WITNESS: A microgram.

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THE COMMISSIONER: Funny initials -

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ug equals microgram.

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MS. CRONK: Q. So that for example

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with respect - I'm sorry, Mr. Commissioner.

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THE COMMISSIONER: A microgram is

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what expression of a gram?

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THE WITNESS: 10 to the minus 6th,

one-millionth of a gram.

19

THE COMMISSIONER: And the nanogram

20

is a billionth I suppose?

21

THE WITNESS: 10 to the minus 9.

22

THE COMMISSIONER: So 10 micrograms

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is still vastly less than a nanogram?

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THE WITNESS: 10 micrograms is

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vastly more than a nanogram.

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THE COMMISSIONER: A microgram, yes,  
that is what I mean. In fact it is what, 100 times?

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THE WITNESS: No, one microgram is  
a thousand times more than a nanogram.

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THE COMMISSIONER: Yes, but 10.

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THE WITNESS: 10 would be 10,000 times  
more than a nanogram.

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THE COMMISSIONER: But your  
interpretation is that the more that you have to  
add in order to get this cross-reactivity means of  
course the less cross-reactivity there actually is?

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THE WITNESS: Yes.

THE COMMISSIONER: Do you have any  
doubt about your interpretation? You say it is your  
interpretation. Do you have any serious doubt about  
it?

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THE WITNESS: It is possible that  
Abbott have converted all readings to nanograms per  
ml, one nanogram per ml and have evaluated it in  
that light. I think they would have misrepresented  
the data somewhat if that is the case.

MS. CRONK: Q. Without otherwise  
indicating on the face of the document that that  
had been done, and that indication is not contained





1  
2 in the document, I take it?

3 A. I have not seen it in the  
4 document.

5 THE COMMISSIONER: The reason  
6 that you might suspect that they have converted is  
7 that the cross-reactivity is so low in some of them  
8 that it would be hard to get much lower.

9 THE WITNESS: That indicates a  
10 specific antibody, which is what they are trying to  
11 show they have.

12 MS. CRONK: Q. Dr. Soldin, quite  
13 apart from the compounds indicated on this list, do  
14 you have any knowledge as to whether the Abbott  
15 Company undertook and conducted a cross-reactivity  
16 test in respect of either quinidine or propanolol?

17 A. No, I do not.

18 Q. Have you, sir, in your  
19 laboratory since either using the FPIA method on  
20 an experimental evaluative basis, or since using it  
21 on a full time basis, since March of this year,  
22 conducted any cross-reactivity tests of your own to  
23 either compare the results with what is disclosed  
24 on this table or to include compounds not listed on  
25 this table?

A. We have done one or two





1  
2 cross-reactivity studies on the RIA technique but not  
3 at this point in time on the FPIA technique.

4 Q. If we turn to the top of the  
5 next page of this document, Dr. Soldin, a category  
6 entitled "Sensitivity" I note that the document  
7 states:

8 "The lowest measureable level is  
9 defined as that concentration which  
10 can be distinguished from zero with  
11 95 per cent confidence; it was deter-  
12 mined to be 0.2 ng/mL."

13 Do I correctly take it that that is  
14 the reference provided by the Abbott Company to what  
15 they consider to be the minimum detection level of  
16 the FPIA system, using this antibody?

17 A. Correct.

18 Q. But you have told us that for  
19 your purposes in your laboratory you are using the  
20 same minimum detection level that has been used  
21 for the RIA system, that is .5?

22 A. Correct.

23 MS. CRONK: Sir, could we mark  
24 this document as the next exhibit, please?

25 THE COMMISSIONER: Exhibit 24.

---EXHIBIT NO. 24: Document entitled "Cardiac  
Glycoside Drug Assays - TDX  
Digoxin".







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MS. CRONK: Q. Dr. Soldin, we have heard evidence from Dr. Ellis and in passing from yourself this morning that in January of 1982 there was occasion in the hospital to run digoxin assays on patient samples in respect of patients who had not been prescribed digoxin.

Were you involved in the conducting of those tests?

A. My laboratory was involved, yes.

Q. Did you supervise those tests?

A. Correct.

Q. Can you tell me, Dr. Soldin, first, how did it come about that those digoxin assay tests were undertaken? We are talking now January of 1982.

A. There were some five infants that became ill at the same time on Ward 7F and there was no explanation for them becoming ill. Because of the sensitivity of the Hospital to digoxin and its past history, we thought it appropriate to measure the digoxin concentrations in these children and subsequently, actually, on the whole ward.

Q. Stopping there for a moment,





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what is Ward 7F in the Hospital?

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A. It is a Neonatal Ward.

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Q. Is that what it was in January

5

of 1982?

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A. Right.

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Q. When you say that five of

8

these children became ill at the same time and there

9

was no ready indication as to why they had become

10

ill, did they become ill in the same way? Were

11

they exhibiting the same symptoms? Was there some

12

commonality in what they were exhibiting?

13

A. Apparently - right. There

14

seemed to be some similarity in the symptoms.

15

Q. Do I take it that none of

16

those five children had been prescribed digoxin in  
the hospital?

17

A. I think that is correct. One

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of the children actually ---

19

Q. Dealing just with the five

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first that became ill ---

21

A. My problem is, I'm not sure

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whether Hamblin was one of those five. There was  
one patient ---

23

Q. I'm sorry, Hamblin?

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A. Hamblin, H-a-m-b-l-i-n. There

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was one patient by that name who was receiving digoxin and whose concentrations were measured and were therapeutic but the rest of the patients on that ward were not receiving digoxin.

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Q. Perhaps to be clear about this, Dr. Soldin, how many patients in total from that ward, how many were involved in the tests?

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A. There were some 15 of them.

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Q. Was that the total ward population at that time?

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Q. Were the five that you described as having become ill and exhibiting the same clinical symptoms part of that group of 15 or are they in addition to the group of 15?

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A. They are part of the group.

Q. Of the 15, as I understand what you have just said, one of the 15, the child you have just described, was on prescribed levels of digoxin?

A. Correct.

Q. And he may or may not have been one of the five that exhibited the same clinical symptoms of illness?

A. Correct.







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Q. Did any of the other 10 appear to be overtaken by the same symptoms that were exhibited by the first five that you have described?

A. No.

Q. How old were these patients, in approximate terms? They were on the Neonatal Ward.

A. I don't have their record here but they were young infants.

Q. We have had a number of varying definitions of neonate put forward, Dr. Soldin, and I appreciate that that definition is perhaps in the eye of the professional who is asked to make the judgment. In your view, can you approximate for us, were any of these children over six months of age?

A. I think they were all younger than six months.

Q. Can you help me, again I wish to be fair to you, can you help me as to whether or not they were older than - are we talking the first month or two of life or are we talking something older than that?

A. Most of them would have been under two months. Were they all under two months is something I cannot be sure about unless we look





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at the records.

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Q. The assays that were conducted, you have described and told me were digoxin assays, and that they were undertaken because of what I think you described as the sensitivity to the prior experience in the Hospital. Were the assays that were undertaken done on ante mortem or post mortem samples?

A. They were done on ante mortem samples.

THE COMMISSIONER: None of them died, did they?

MS. CRONK: Q. Did any of them die, Dr. Soldin?

A. One of them died.

Q. In respect of the one that did die, were they ante mortem or post mortem samples?

A. They were post mortem.

Q. So with the exception of that child, the others were all ante mortem samples?

A. Correct.

Q. What type of samples were tested?

A. Serum or plasma.

Q. No whole blood?

A. No.





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Q. And no cord blood samples  
involved?

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A. No.

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Q. And clearly no tissue samples  
involved?

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A. No.

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Q. Did any of these children,  
the 15 children, to your knowledge at the time these  
tests were conducted, have diagnosed cardiac problems?

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A. One of them was on digoxin,  
so I take it that one of them would have had some  
problem.

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Q. All right.

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A. The rest, I'm not aware of  
a problem but again I would ask you to ask the  
clinician on that ward, looking at the case histories.

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Q. Am I correct that at the time  
that these tests were conducted the requisition  
form that has been admitted as an exhibit before  
the Commission for digoxin assays pursuant to the  
Therapeutic Drug Monitoring Program would have been  
in place? This is January of 1982; or do you know?

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A. The requisition I think was in place in January of '82. I'm not 100 per cent sure of that. It was certainly in place in February of '82. I would have to check up whether it was in place in fact of January of '82.

Q. All right. Well, what I'm getting at, Dr. Soldin, is simply this. I'm referring to Exhibit 15A, that's the first requisition form that was introduced with, we have heard, the Therapeutic Drug Monitoring Program and on the face of that requisition there's a space for various information to be inserted by the physician who is requesting a particular assay to be conducted and amongst the various categories of information is the category of, first of all, the particular drug in respect of which the assay is being requested must be indicated on the form and, as well, there is a space for an indication as to the time of the administration of the last dose. Do you have that before you, sir?

A. No, I don't. But I know the requisition, right, you're correct.

Q. Well, sitting here today and so far as you are aware, leaving aside the one child who was receiving prescribed levels of digoxin,





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were any of the other 14 known by you or by those you supervised in your laboratory to be patients suffering from cardiac ailments, cardiac patients?

A. I didn't have that knowledge, no. But none of the other patients were known to be on digoxin.

Q. All right. And similarly, at the time that these tests were conducted, to your knowledge, did any of these patients, any of the 15 suffer from kidney impairment or any renal dysfunction?

A. Again, not to my knowledge.

Q. How many assays were run for digoxin in respect of each child, Doctor?

A. Well, on the five children two runs were performed, two assays, in other words, on different samples drawn at different times.

Q. All right. Dealing just with that then for the moment. I take it because the FPIA system was not in place in the hospital at that time, unless it was the month of January, 1982 coincidentally when it was there for evaluation procedures, that these assays were conducted by the RIA methodology?

A. Right.





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Q. And when you say that two different samples were involved, on the first assay that was done, do you recall whether they were plasma or serum samples?

A. They were serum or plasma, I can't tell you which.

Q. All right. And on the second, the same thing?

A. The same thing, right.

Q. All right. Do you know the difference in time today or do you recall the difference in time between when the second assay was run?

A. They were approximately six hours later.

Q. All right. What about the other ten children, how many assays were done in respect of them?

A. One. Well, each assay, as you know, is done in duplicate.

Q. One duplicate assay?

A. One duplicate assay.

Q. And in respect of the other five, two duplicate assays?

A. Two duplicate assays.







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Q. In respect of each?

THE COMMISSIONER: The five sick ones.

THE WITNESS: The five sick ones, right.

THE COMMISSIONER: I imagine though all the children were sick or they wouldn't have been in the hospital, but these were particularly sick, these five?

THE WITNESS: Yes.

MS. CRONK: Q. Can you tell us, Dr. Soldin, dealing now just with the five children that you have described, the first category on the first digoxin assay, what were the recorded levels for digoxin, if any?

A. I'm sorry, I will have to find that.

Q. Well, if you could take a minute, Dr. Soldin, I'm going to ask you what the recorded levels were on the first assay for the five children, what they were on the second assay and what they were on the assay for the other ten children.

THE COMMISSIONER: I take it the levels would be different. Have we a schedule of





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any kind?

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MS. CRONK: I do not, sir.

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THE COMMISSIONER: Yes, all right.

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THE WITNESS: Well, let me read  
you the results on the first assay. Baby boy Gee.

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THE COMMISSIONER: I'm sorry, you  
will have to do this slowly.

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THE WITNESS: G-E-E, okay.

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MS. CRONK: Well, if I could  
make a suggestion, Mr. Commissioner. I'm not sure  
that anything turns on the identity of these  
children.

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THE COMMISSIONER: No, no, no.

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MS. CRONK: Q. Could I ask that  
you simply read the readings off from the first  
assay on these five children without indicating  
their names?

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A. Well, 0.4, 0.4, 1.3.

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THE COMMISSIONER: Perhaps you  
could give us - are they ---

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THE WITNESS: 2.1. I'm just trying  
to get the sequence. 0.6.

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MS. CRONK: Q. All right.

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A. I'm sorry, there was a sixth  
one, Gee, 0.8.

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K-6

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Q. Well, can you help me --

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A. So, we did six in duplicate.

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Q. All right. So that one of

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the children that was done in duplicate was not of

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the group of five who shared the same clinical

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symptoms, or are we talking about six children who

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became ill and shared the same clinical symptoms of  
illness?

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A. You know, I'm not sure if

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there were five or six that became ill. There was

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one of these was a set of twins.

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Q. Oh, all right.

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A. Okay.

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Q. Is it possible that the set

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of twins was counted as one when you told me about  
the five who became ill?

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A. I'm not sure if five or six

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came down with the same clinical symptoms.

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THE COMMISSIONER: That's one assay  
on six babies, is that right?

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THE WITNESS: Sir, I have given you---

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THE COMMISSIONER: The second assay?

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THE WITNESS: One assay on six

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babies, right.

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THE COMMISSIONER: Now, could you

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Soldin, dr.ex.  
(Cronk)

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give us the second assay on these?

THE WITNESS: So, the second one was 0.4 for the first one that I have quoted.

MS. CRONK: Q. i.e., the same level that had been referred on the first assay?

A. The same, right.

Q. And the second?

A. 0.4.

Q. The same as had been recorded on the first assay?

A. Right. 1.3.

Q. Again, the same?

A. Right. 1.4.

Q. Now, is that a drop in respect of the patient who had previously recorded 2.1?

A. Right. This was the patient known to be on digoxin.

Q. All right. And the next?

A. 0.4.

Q. Is that a drop from the 0.6 reading on the previous assay?

A. Correct.

Q. And then the last one?

A. 0.4.

Q. And again, that's a drop from





K-8

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the reading of 0.8 on the first assay?

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A. Correct.

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Q. Right. Dr. Soldin, if we

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leave aside for the moment the patient who was

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known to have been prescribed digoxin, that child

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had initial readings of 2.1 and 1.4 on the second

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assay. The highest reading of the group of the

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remaining five that you obtained I take it was

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the 1.3, and that was consistent on both assays?

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A. That's right, yes.

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Q. All right. And of the other

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four, two readings consistently on both assays

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were less than .5 nanograms?

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A. Right.

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Q. Right. And the other two on

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the first assay were slightly over .5 but on the

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second assay again dropped both of them to less

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than .5 nanograms?

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A. Correct.

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Q. Right. Now, in respect to

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the other ten patients in respect of whom one assay

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was run, can you tell me, without any inconvenience

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particularly, what the results of those recordings

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were?

Let me start this way. Were there





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any readings on those ten patients that were in excess of .5?

A. No, there were none over .5.

Q. All right. And when you previously told me, Dr. Soldin, that in respect of the group of six that a second assay was run on different samples - I'm sorry, a second assay was run on different samples, were they, and I may have asked you this and if I did please forgive me, were they the same kinds of samples, i.e., plasma or serum as had been applicable on the first instance?

A. Right, right.

Q. Right. Are you familiar, Dr. Soldin, with the report prepared by the Dubin Review Committee with respect to the Hospital for Sick Children released in January of 1983?

A. I've read most of that.

Q. Are you familiar, sir, with that portion of the report which speaks about the events that occurred in January of 1982 on Ward 7F of the Hospital?

A. Right.

Q. Perhaps your counsel could get you that.







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I draw your attention to page 178,  
sir.

THE COMMISSIONER: Unfortunately,  
I left it and I asked the poor fellow to go and  
get the Dubin Report, forgetting that there is  
nothing about Dubin on the front of it at all.

MS. CRONK: Q. I draw your  
attention, Dr. Soldin, to page 178 of the report  
if I could.

A. Right.

Q. In that section of the report,  
the illness of these five children that you have  
described to us this morning is also described, and  
with respect to the child upon whom a 1.3 digoxin  
recording was made, it is suggested that that  
reading was the result of an error in drug  
administration, that is, it is suggested that there  
was a medication error and digoxin was prescribed  
to that child when it was intended for another  
child. Can you help me, sir, as to whether, as  
the person who supervised these tests, you have  
any knowledge as to whether that 1.3 reading  
occurred as a result of a medication error, as  
suggested in this portion of the report?

A. No. It could have been as a





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result of the medication error, but it need not necessarily have been as a result of a medication error.

Q. Are you satisfied, sir, that it was, or do you have any knowledge as to that?

A. No. I think that in the light of information which we have today that it could well be that that was not as a result of the medication error.

Q. And if we take for the moment, make the assumption for the moment, I'm not suggesting it is in fact what happened, but if we take the assumption for the moment that it was a medication error, I take it that the highest result that was recorded, or the highest digoxin reading that was recorded for any of these 15 patients was a 0.8 which, on a second assay, was reduced to 0.4 ---

THE COMMISSIONER: I'm sorry, I don't understand what you're saying.

MS. CRONK: I'm sorry.

THE COMMISSIONER: Assuming that it was a ---

MS. CRONK: If we assume that the 1.3 digoxin reading related to a patient who had in





K-12

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fact been administered digoxin ---

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THE COMMISSIONER: Oh, I see, yes.

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The highest would be 0.8, yes. Yes, I think that speaks for itself.

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MS. CRONK: Q. Now, in respect of all of these tests, both the first and second assays conducted on the group of six children, and the one assay run in duplicate on the other children, were all of those samples antimortem samples, Dr. Soldin?

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A. Yes, they were.

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Q. And did the Hospital identify, in the case of the five or six children who became ill, some cause thought to have resulted in the similar illness?

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A. Yes, they did.

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Q. And what was that, sir?

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A. They thought that these children had received epinephrine instead of vitamin E.

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THE COMMISSIONER: I'm sorry, that they had received what?

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THE WITNESS: Epinephrine.

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THE COMMISSIONER: Oh, yes, instead of vitamin E.

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THE WITNESS: Yes.

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THE COMMISSIONER: That's the Murphy

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K-13

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child, was it, that died?

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THE WITNESS: Right.

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MS. CRONK: Q. And did you, sir,  
in supervising the conduct of these tests, run a  
test for cross-reactivity between epinephrine and  
the antibody on the RIA methodology that was being  
used?

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A. Yes, we ran cross-reactivity  
studies on epinephrine and on vitamin E.

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Q. And on vitamin E?

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A. Right.

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Q. With what results, Dr. Soldin?

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A. There was no cross-reactivity,  
measurable cross-reactivity.

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Q. For either?

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A. For either.

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Q. Right, thank you. Now, after  
the tests that were conducted in January of 1982,  
did you have occasion later in that year, Dr.  
Soldin, to run digoxin assays on any other patients  
who were known not to have been prescribed digoxin?

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A. Yes, we did. We were  
interested of course in obtaining values that were  
greater than .2 in many of these children that were  
not receiving digoxin. So, we asked our neonatal





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ward to, whenever they could, send us a sample,  
to send us samples for digoxin analysis on patients  
not receiving digoxin. Three such samples were  
obtained during '82 and the results on all three  
were less than .5.

Q. And in respect for those  
samples, Dr. Soldin, do I take it that those were  
all ante mortem samples as well?

A. They were ante mortem samples,  
right.

Q. And they were as well plasma  
or serum?

A. Right.

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Q. And because it was 1982, are we talking about the RIA methodology as having been employed for those tests, or were any of the three or all of the three conducted on FPIA during the month it was there for evaluation purposes?

A. The RIA methodology.

THE COMMISSIONER: I'm sorry, what was that?

THE WITNESS: RIA methodology.

MS. CRONK: Q. And at the time these tests were conducted, Dr. Soldin, did you have any knowledge or understanding as to whether any of the three patients suffered from cardiac ailments?

A. No, I didn't. The way the study was set up was in a blind fashion. In other words, we were supposed to receive samples without knowing whether or not those patients were on digoxin.

Q. I see.

A. So, that is the way it was set up. We had no knowledge.

THE COMMISSIONER: You said these readings were less than what?

THE WITNESS: 0.5.

MS. CRONK: Q. That is nanograms







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per ml?

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A. Right.

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Q. And similarly, when you indicated they were to be conducted in a blind fashion, do I take that to mean that you were, as well, not provided with particulars concerning their clinical condition?

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A. Correct.

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Q. And that would apply as well to kidney problems as well as to cardiac problems?

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A. Any problems. Those samples came down to the laboratory in the exact same fashion that any other samples would come down, with a requisition saying they wanted a digoxin sample assay.

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Q. And did you, after conducting the tests, determine whether or not any of those children had been on a prescribed digoxin level?

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A. I have had verbal communications with doctors on 7G, yes, which indicated to me that those were the only three samples they sent down to us during 1982 in this study.

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Q. And were any of those three patients on prescribed levels of digoxin?

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A. No, they were not on digoxin.





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Q. After 1982, doctor, dealing with this year because we have heard evidence as well as to the results of these tests on patients who were not known to have been prescribed digoxin, did you have occasion in 1983 to conduct digoxin assays on patients who were known not to have received digoxin?

A. Yes. We have been doing that over the past ten days or so.

Q. Can you tell me, doctor, how many patients have been sampled and tested?

A. Eight patients from our neonatal ward.

Q. Again, Ward 7F?

A. 7G.

Q. And what method was used for the testing of those children's samples?

A. On all eight, the FPIA method was used and, on five of those eight, the RIA method was used.

THE COMMISSIONER: I'm sorry. You said the FPIA on three; is that right?

THE WITNESS: The FPIA method was used on all eight and the RIA method was used on five of the eight. In other words, the exact same samples





Soldin  
dr.ex. (Cronk)

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were analyzed by both methods.

MS. CRONK: Q. We are talking now of tests that have been conducted on eight children in total within the last ten days in your laboratory --

THE COMMISSIONER: I am being very slow on this. What did you say, on all eight of them, you conducted the new method?

THE WITNESS: Correct.

THE COMMISSIONER: What you call the FPIA; is that right?

THE WITNESS: Right.

THE COMMISSIONER: Yes. All right.

MS. CRONK: Q. -- and you used, as I understood it, you just told the Commissioner, Dr. Soldin, the same sample for five of those patients to run a second test on the RIA method in addition to the test or assay that you were running on the new method, the FPIA; is that correct?

A. Right.

Q. And we are talking eight children in total?

A. Eight children in total.

Q. Can you tell me, sir, or do you know what the approximate ages of those children were?







Soldin  
dr.ex. (Cronk)

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A. Again, under two months.

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Q. And what kind of samples were  
obtained?

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A. Serum or plasma.

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Q. Are we talking about ante  
mortem samples or post mortem?

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A. Ante mortem samples.

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Q. And what were the results,  
first, Dr. Soldin, dealing with the five assay  
tests done on the five children by the RIA method?

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A. One result was over 0.5,  
four of them were below 0.5. The one that was over,  
was 1.4.

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Q. I'm sorry?

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A. Nanograms per ml.

Q. Let's go through that again,  
Dr. Soldin, if we could.

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Of the five tests that were conducted  
on the RIA method, I understood you to say that four  
readings were less than 0.5 nanograms per ml; is  
that correct?

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A. Correct.

Q. And one reading was 1.4 nano-  
grams per ml?

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A. Correct.





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Q. And that is the only one of that group of five on the RIA method that was over .5 nanograms?

A. That's right.

Q. Now, let's deal with the FPIA test results on all eight children.

Can you tell us what the recorded levels were there?

A. Seven of the eight were less than 0.5 and one was 0.9 nanograms per ml.

Q. 0.9?

A. Correct.

Q. And was the child, Dr. Soldin, the sample that recorded 0.9 on the FPIA, the same child that recorded 1.4 on the RIA?

A. Yes.

Q. So I take it, at least in respect of that sample, the FPIA reading was lower than the RIA reading?

A. That is right.

Q. And to what, if anything, can you presently attribute that, Dr. Soldin?

A. Well, there are several possibilities. One is that the antibody is more specific, the antibody used by the FPIA procedure,





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more specific with respect to whatever compound is being measured.

Another possibility is that, because we are deproteinizing in the FPIA method, we are deproteinizing - in other words, we are removing the proteins --

Q. Thank you.

A. -- we may be removing a compound that cross-reacts with the antibody and you wouldn't measure that by the FPIA method because we have no proteins there.

Q. But you would measure it with the RIA method?

A. But you might measure it, right.

Q. Now, am I correct, Dr. Soldin, that in respect of all these eight children, in all of these test results, taking into account even the highest - which was the 1.4 on the RIA and the same child being the .9 on the FPIA - that all of those recorded readings are within what would be considered the therapeutic range for digoxin had it been administered?

A. No. The therapeutic range is 0.8 to 2.0 nanograms per ml.

Q. That's right.







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A. And a lot of these kids had values below 0.5; so, they were outside the therapeutic range.

THE COMMISSIONER: They were sub --

MS. CRONK: I'm sorry.

Q. They were sub-therapeutic or within the therapeutic range.

A. Right.

Q. And that would apply as well to the tests that were conducted that you described a few moments ago in 1982 on the three patients sampled?

A. Yes.

Q. And, as well, it would apply to the test results in January of 1982?

A. That is correct.

THE COMMISSIONER: There was one at 2.1 - it is all a matter of record.

THE WITNESS: That's right.

THE COMMISSIONER: The 2.1, it depends on what standards you use. If you use 2.0 as the limit of the therapeutic range...

MS. CRONK: Q. The 2.1, as I understand it, was indeed in respect of a child who had been prescribed digoxin, and you are quite right,





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in the range that you have described, Dr. Soldin,  
that would be slightly above the therapeutic range.

A. Right.

Q. That is the one that was  
also reduced on the second assay?

A. Right.

Q. Now, all of these tests and  
assays, as I understand it, Dr. Soldin, were con-  
ducted on ante mortem samples, all of them?

A. That is right, yes.

Q. Now, as I understand it, there  
have, in fact, been - and please correct me if I am  
wrong - post mortem sampling or assays done for  
digoxin in the Hospital since March of 1981?

A. Yes.

Q. And have some of those assays  
been conducted in your laboratory?

A. Yes, they have.

Q. At whose request were those  
particular samples analyzed, those assays undertaken?

A. At the request of the patho-  
logist.

Q. And was that more than one  
pathologist or are we talking about one doctor  
specifically?





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THE COMMISSIONER: I thought it was  
a matter of routine. Am I wrong about that?

MS. CRONK: That is what I am coming  
to, Mr. Commissioner.

Q. Were these assays conducted  
at the request of one particular pathologist at the  
Hospital or a number, as a matter of routine?

A. It became a matter of routine,  
I think, after March of 1981, to measure digoxin  
in all autopsy samples if the samples came to us,  
obviously, from the Pathology Department.

Q. Perhaps my understanding is  
incorrect. Did they come to you from any particular  
doctor or pathologist?

A. From a number of doctors.

Q. Now, when I asked you, Dr.  
Soldin, whether those tests were conducted from  
March of 1981 forward, are they still being con-  
ducted as at today's date?

A. That is correct.

Q. And were any of those tests or  
assays, in fact, undertaken in the latter part of  
March of 1981?

A. I think they were, yes.

MS. CRONK: Mr. Commissioner, as you







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might anticipate, I have had an opportunity to discuss this particular matter with Dr. Soldin before he came today to give evidence.

It is the proposal of Commission Counsel that Dr. Soldin, or Dr. Phillips, a Pathologist from the Hospital For Sick Children, will be called to give evidence in detail regarding both the conduct of these post mortem assays for digoxin and as to the test results realized.

The reason for that is that it is Commission Counsel's understanding that many of these post mortem tests, in fact, coincide with the month of March 1981 and several of the children with whom, sir, you are concerned in the inquiry period and, rather than deal with those at this stage, we propose to deal with all of the post mortem digoxin assay tests on children known not to have received digoxin in one grouping through one witness at a later date.

THE COMMISSIONER: Yes. All right. It becomes a very fine line, of course, because we want to know, I would think, in this part of the inquiry just what the results were generally.

Can we not ask a question to know generally what was the highest - We all know about





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Baby Murphy, that there was an inquest a little while ago - what was the general range, the highest range that you obtained.

MS. CRONK: Sir, I don't mean to interject, and please excuse me. Some of the ranges that I understand will be given to you in response to that question are, indeed, what have been perceived to be the very high ranges on the children that were tested in March of 1981.

I understood from Dr. Soldin that he would have difficulty on this particular day in telling us, for example, what the highest was on children outside the March 1981 time period.

If I am wrong, Dr. Soldin...

I am entirely in your hands, Mr. Commissioner. If you would like that evidence led now, I am prepared to do so.

THE COMMISSIONER: Obviously, you don't want that, so I am not going to press it.

MR. STRATHY: If I might make one observation and that is as it relates to the FPIA method. It had been my understanding that Dr. Soldin had used FPIA on autopsy samples and that one of the factors influencing his views on FPIA was the results on autopsy samples, or at least that was my under-





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standing. He might be able to give his evidence on autopsy samples on FPIA.

THE COMMISSIONER: It is going to be very difficult then, Miss Cronk, to keep this out. Is there not some kind of a chart that we have? Not the babies which we are inquiring about, but the other babies? The other babies are regular post mortem examinations. Those figures are not available, I take it?

MS. CRONK: Well, the difficulty, as I understand it, sir - and, again, if Dr. Soldin has the information today and is in a position to provide it for us, I have no difficulty in exploring that area. My understanding was, though, that many of these assays were undertaken at the request of Dr. Phillips, the Pathologist at the Hospital, and that Dr. Phillips was the appropriate individual to give evidence concerning the results as a whole.

If my understanding in that regard is mistaken, we can deal with those autopsy results right now.

THE COMMISSIONER: Well I don't know what sort of a task it is. Is it going to take hours to get it or is it just going to take minutes. What is it?







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MS. CRONK: Well, Mr. Commissioner,  
in any event, it was going to be my suggestion that,  
when we break for the noon break, with Miss Devin's  
concurrence - and I don't have prior authority for  
this, but with her concurrence and Dr. Soldin's  
willingness that Dr. Soldin make himself available  
at this stage for various questions from other  
counsel.

THE COMMISSIONER: That's fine.

MS. CRONK: And we can perhaps ex-  
plore this issue then.

THE COMMISSIONER: You are now, as  
plotted; you are finished?





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MS. CRONK: There is one small area, about five minutes, Mr. Commissioner, and I propose to deal specifically - if we could I suggest we break now and let other counsel have the benefit of learning from Dr. Soldin what I have learned about these autopsies.

THE COMMISSIONER: Could we just know what this small area is?

MS. CRONK: I am sorry. The only area left that I intend to explore with Dr. Soldin relates to recovery rate studies that he has conducted in respect to the RIA tests at the Hospital, and the FPIA tests.

THE COMMISSIONER: Yes, all right.  
Yes, Mr. Buhr?

MR. BUHR: Could I just interject, Mr. Commissioner. I assume from Dr. Soldin's evidence that the major reason for this whole testimony about the FPIA and clearly he has already indicated that one of his concerns is from the results of these autopsy reports so hopefully I would ask that the Doctor acquaint himself with these studies over the lunch period because it makes it very difficult to cross-examine him on that area at all if he is not really up to date on it.





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MS. CRONK: I think perhaps, Mr. Commissioner, we can resolve the issue this way. We know that the FPIA methodology has only been in use in the Hospital on a full-time basis since March of this year. Perhaps I can direct Dr. Soldin's attention to the particular autopsy --

THE COMMISSIONER: That is not what is worrying me and I do not think it is what is worrying anybody else. It is that this, presumably, from the routine post mortem examinations of these babies who died, you cannot have a post mortem examination unless the baby did die, there are figures available as to the digoxin levels. That is surely what we want to know. These are not the babies who are under inquiry now. Now, if you do not want to give it to us I suppose I can play the game and forbid the cross-examination, but it seems to me that that would be most important.

MS. CRONK: It is not a question at all of not wanting to provide it, Mr. Commissioner. I had understood that Dr. Soldin did not have those full figures available today and what I would propose to do, if it would at least resolve some of my friends' dilemma, so that they could have a full and complete cross-examination of Dr. Soldin with respect







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to this particular methodology, is to ask him to acquaint himself over the noon hour, if he does not have it already, with those autopsy post mortem sampling results that he looks to in support of his judgment as to the efficacy and desirability of the FPIA test, if that can be done.

THE COMMISSIONER: I don't know, can it be done, Doctor?

THE WITNESS: I have the data here with regard to the FPIA tests and I could talk about it right now if you wish.

THE COMMISSIONER: Have you got the figures? Have you got the figures for the routine post mortem examinations for digoxin after March of 1981?

THE WITNESS: I do not have all the figures.

THE COMMISSIONER: Just a minute. Yes, Mr. Bogart?

MR. BOGART: I do not know if this is helpful, Mr. Commissioner, but I am trying to be helpful. At least in respect to readings in excess of 5 on autopsy samples taken since March of 1981, I believe that is contained in Volume 13 of Dr. Ellis' testimony at the preliminary inquiry, starting at page 12.





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If that will help Dr. Soldin and Miss Cronk, I simply raise that for that purpose. You remember I referred to that yesterday.

THE COMMISSIONER: Yes. I think what we might do, what about your considering this problem. It is a matter of considerable interest and I do not see why that is not included in this aspect of the Inquiry because it does not involve these particular children. When we do get to the particular children we want to know what the readings were with other children who have died since that time and for which there is no suspicion of foul play.

MS. CRONK: I quite agree, Mr. Commissioner, and if Dr. Soldin has that information available --

THE COMMISSIONER: Do you want to see if you can get that? Now, the other thing I was wondering is about - you have not consulted with him yet or with his Counsel. Who is acting - what is your position with regard to --

MS. DEVINS: I am acting and will be acting for Dr. Soldin.

THE COMMISSIONER: Would you consult with him and determine whether he is willing, after the examination is completed, I think we will come





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back here at 2:30 to complete the examination and then perhaps we might, I don't know, we will decide then whether we will take the rest of the afternoon, if Dr. Soldin is willing, for the informal examination, or whether we will start the cross-examination later on this afternoon.

MS. DEVINS: Fine, Mr. Commissioner.

MR. BOGART: Sir, can I ask one more thing?

THE COMMISSIONER: Yes.

MR. BOGART: This is the point I raised yesterday with respect to the transcripts of Dr. Ellis, Volume 13, beginning at page 12, my understanding is there are also some reports in respect of ante mortem readings in excess of 5. I believe that to the extent that we would be interested in autopsy --

THE COMMISSIONER: But the routine examination was post mortem. There was no routine ante mortem examination.

MR. BOGART: That is what I was not clear about yesterday, sir. My understanding from the transcript is that there were over 3,000 of these tests done.







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I am just raising that, sir, because  
if you deem it relevant at this point I would like to  
ask some questions about it. If it is not relevant  
at this point, I will ask them later.

THE COMMISSIONER: Well, let us see  
what we come up with at 2:30.

--- Luncheon adjournment.





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---Upon resuming at 2:30 p.m.

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THE COMMISSIONER: Yes, Ms. Cronk.

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MS. CRONK: Q. Dr. Soldin, you

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will recall before the break we were discussing

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a series of ante mortem samples that had

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been taken from patients known not to have received

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digoxin and in respect of which digoxin assays had

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been run. Do you recall that discussion?

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A. Right.

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Q. I would like to talk for a

12

moment about the ante mortem testing results that

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we were discussing earlier and then I will return

to the post mortem testing.

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You told us this morning that they

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were, as I understood it, five samples tested on

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both the RIA and the FPIA method. Is that correct?

17

A. Correct, yes.

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Q. Can you tell us, because you

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gave us the recorded levels of those tests, can

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you tell us whether the levels recorded were lower

pursuant to one technique versus the other on those

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five samples?

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A. The results were lower by the

FPIA method.

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Q. Are you able today, sir,

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2 to give us a breakdown as to what the results were  
3 by FPIA versus RIA?

4 A. I do not have those numbers  
5 here but I could certainly get them. The mean  
6 result was definitely lower by the FPIA method.

7 Q. On all five?

8 A. The mean result. I think all  
9 five were lower, yes.

10 Q. As I understand it, you do not  
11 have a particular breakdown with you today but you  
12 will provide it to us?

13 A. Certainly.

14 Q. Thank you.

15 Can you tell, Dr. Soldin, were those  
16 five samples that we have talked about the only  
17 ante mortem samples from patients known not to have  
18 received digoxin which were available to you for  
19 comparative testing? In other words, are they the  
20 only ones on which you have run tests both on the  
21 RIA and the FPIA, ante mortem?

22 A. The patients who were not on  
23 digoxin, you mean?

24 Q. Yes.

25 A. They were the only ones that  
I currently have a comparison of the two techniques.







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Q. Again, those samples related  
to patients known not to be on digoxin?

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A. Correct.

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Q. Have you had occasion since the  
introduction of the FPIA technique to the Hospital  
in March of this year to do a comparative study run,  
if I can express it that way, on ante mortem samples  
of patients known to be receiving digoxin?

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A. Yes, I have.

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Q. Can you tell me, first,  
Dr. Soldin, how large that sample group was?

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A. There were 36 samples in that  
group. Both the RIA and the FPIA methods were  
used. Comparison data is summarized in a memo  
that I sent to Dr. MacLeod on the 15th of June.

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Q. 15th of June of this year?

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A. Of this year.

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Q. I have the memorandum in front  
of me, Dr. Soldin, which is dated June the 15th,  
1983 expressed to be from yourself to Dr. MacLeod,  
Clinical Pharmacology, on the subject of digoxin  
measurements.

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Is that the memorandum to which you  
were just referring?

23

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A. It is, yes.

25





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2 MS. CRONK: Could that be marked,  
3 sir, as the next exhibit, please?

4 THE COMMISSIONER: Exhibit 25.

5 ---EXHIBIT NO. 25: Memo from Dr. Soldin to  
6 Dr. MacLeod dated June  
7 15th, 1983 re Digoxin  
Measurements.

8 MS. CRONK: Q. In respect of  
9 those 36 samples, Dr. Soldin, were the same samples  
10 tested on both the RIA and the FPIA techniques?

11 A. They were, yes.

12 Q. What type of samples were they?  
13 We know that they were ante mortem samples, but  
14 were they whole blood, plasma ---

15 A. They were serum or plasma  
16 samples.

17 Q. Are you in a position to  
18 describe for the Commissioner what the comparative  
19 results were in respect of those samples on both  
20 methodologies?

21 A. The methods compared exceedingly  
22 well in that study. The mean results by the RIA  
23 method expressed in nanograms per millilitre was  
24 1.19. The mean results by the FPIA expressed in  
25 nanograms per millilitre was 1.15. The results in  
the actual memo were in nanomoles per litre.





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Q. Where do we find that in the memorandum, Dr. Soldin?

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A. It is on the second page, at the top of the page.

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Q. There are three sections of tabular results on this page - those on the top.

8

A. Right.

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Q. And they are there expressed, I believe you said in nanomoles.

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A. As typed, yes, in nanomoles, and I have converted them into nanograms for you.

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Q. So the RIA mean result shown as 1.53 would be in nanomoles, which you refer to as 1.19. Correct?

14

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A. Correct, 1.19 nanograms.

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Q. And similarly the mean result on which you have described here as TDX, and I take that to be the FPIA method, is expressed in nanomoles at 1.48 and converted to nanograms - that would be, I think my notes says that you said 1.15 nanograms?

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A. Right.

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Q. Can you help us today, Dr. Soldin, as to whether or not ---

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THE COMMISSIONER: Sorry, I'm

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having trouble. 1.53 for ---

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MS. CRONK: The RIA.

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THE COMMISSIONER: Yes, and 1.48?

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MS. CRONK: The TDX.

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THE COMMISSIONER: If we do this

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in nanograms it is ---

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MS. CRONK: 1.19 for the RIA.

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THE COMMISSIONER: 1.19 - oh, I see,  
now it makes sense. Thank you.

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MS. CRONK: You are welcome.

11

Q. Can you help us today,

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Dr. Soldin, with whether or not the patients from

13

whom these 36 samples were drawn were all of the

14

same age group or age range, or do you know?

15

A. No, it is exceedingly unlikely  
that they were the same age group.

16

Q. Were any of them neonates?

17

A. I cannot tell you. I would

18

doubt that, because we needed quite a lot of samples.

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Q. Were all of these samples

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tested in your laboratory, Dr. Soldin?

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A. They were tested in our

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laboratory, yes.

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Q. All right.

And can you tell me, of the 36 samples tested by both methods, what was the highest reading which you obtained on the RIA method?

A. The highest reading was 2.3 nanograms per millilitre. Again, in the graph it is in nanomoles per litre; so, it is a bit confusing.

Q. Where is that shown on the graph?

A. It is page 3.

Q. That is the graph where various items are plotted with RIA shown on the bottom axis of the graph?

A. Yes.

Q. And what is shown on the left-hand side of the graph?

A. The FPIA method.

Q. All right.

So that the highest reading on RIA that you obtained was 2.3 nanograms per millilitre?

A. Right.

Q. What was the highest FPIA result that you obtained?

A. It was 2.2 nanograms per millilitre.





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Q. Well, can you explain for us, Dr. Soldin - or do I take it correctly that the graph, which is page 3 of this memorandum, is a plotted reflection of the results that you obtained by both methods on these 36 samples?

A. That's right.

THE COMMISSIONER: I guess that's clear. The one I'm looking at seems to have all sorts of axes up around the --

THE WITNESS: Each axis represents a sample, yes.

MS. CRONK: Q. Can you tell us, Dr. Soldin, how we distinguish on this graph between an RIA tested sample and an FPIA tested sample?

A. Well, each sample was tested by both methods. You then plot the value you get on the RIA axis versus the value you get on the FPIA axis.

Q. And there appears to be a dotted dividing line or an axis through the graph. Are the axes which appear below it the RIA results?

A. No, no. All of the results plotted have been done by both methods.

Q. Yes.





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A. And we then plot the axes  
and then you work out by what is the best fitted  
line to this, to these series of plots.

Q. All right.

Well, in looking at this graph, if  
we wished to know the results obtained by the FPIA  
technique, how could we identify which were the FPIA  
results?

A. They would be on the left, on  
the left-hand side axis.

Q. All right. And the RIA  
on the right?

A. RIA on the bottom, right.

Q. All right. Thank you.

Now, returning to page 2 of the  
memorandum, Dr. Soldin, in tabular form --

THE COMMISSIONER: I don't know whether  
it matters but I am left completely in the dark with  
this graph. I just don't understand it at all.

The first thing you said, the highest  
that you got on the RIA is 2.3; is that what you said?

THE WITNESS: In nanograms, yes.  
The results are plotted in nanomoles. The Hospital  
switched to nanomoles on April 4th.

MS. CRONK: In an effort to make it







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clearer, sir, I may have made it more confusing.

THE COMMISSIONER: No, no, you didn't. But, sometimes, you have particularly dense objects!

For the first time in my life, I have sympathy for the anti-metric group!

This is -- it just makes it vastly more difficult, but this thing is plotted in these nanomoles?

THE WITNESS: Yes.

MS. CRONK: I asked Dr. Soldin for what I hoped was the ease of reference to convert the two highest readings into nanograms, and those were, as I understand it, the 2.3 reading on the RIA and the 2.3 on the FPIA.

Q. If we could turn then, Dr. Soldin, to page 2 of the memorandum and the tabulated results which appear in the middle section, could you explain to us what the results reflect?

A. Well, both the middle and the bottom section reflect the between-day precision as obtained in our laboratory for both the RIA and the FPIA methods.

Now, the FPIA is labelled as TDX in this memorandum.





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2 Q. And they relate as well to the  
3 same 36 samples?

4 A. No, no. These are between-day  
5 precision studies. These 36 samples were not  
6 analyzed every day for twenty days, but different  
7 quality control materials were analyzed every day  
8 for twenty days and for nineteen days with the FPIA  
9 method, as you can see.

10 n=20 means that they were assayed  
11 20 times once a day for twenty days. n=19 means  
12 they were assayed once a day for nineteen days, and  
13 the mean results are shown again in nanomoles per  
14 litre for these three different quality control  
15 serums, and you can see that the results are fairly  
16 close for the RIA and for the TDX or FPIA method.

17 The precision data again reveals  
18 that what we have plotted here is a coefficient  
19 of variations, which is a measure of the precision.

20 If you want me to go into more depth  
21 on that, I would be happy to do that.

22 Q. Well, all right. Let me deal  
23 with this for a moment.

24 What does the data shown in that part  
25 of the table, that is, the second tabular section,  
indicate to you in respect of the FPIA method versus





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the RIA method? What does it tell you?

A. In the second section, it tells me that the precision of the two procedures is comparable at three different concentrations of digoxin and that the accuracy of the method at those three concentrations is also comparable.

Q. And the lower section of the tabulated result in the bottom of that page?

A. That was another precision between that precision study, again, at three different concentrations and, really, the interpretation of that table is the same as the middle.

Q. So that the precision of both methods on these studies was very close to each other?

A. Right.

Q. Now, leaving aside for the moment, Dr. Soldin - and I will return to this memorandum - the question of ante mortem samples. Turning now to post mortem samples. Since the introduction of the FPIA methodology in the Hospital in March of this year, have you had occasion to do comparative testing on post mortem samples for digoxin on both the FPIA and the RIA methods?

A. Yes, I have.







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Q. And how large was the sample group you have used for those purposes?

A. I am just trying to find it.

Q. That's fine.

A. I believe we have analyzed 37 samples by both procedures, autopsy samples.

Q. They were all autopsy samples?

A. Is that not what you asked?

Q. Well, no, I used the word "post mortem". Were they all autopsy samples?

A. They were, as far as I know, yes.

Q. And were these samples again plasma or serum?

A. Correct.

Q. And the same samples, that is, all 37, I take it, were tested on both the RIA and the FPIA?

A. They were.

Q. Can you help us as to whether or not the patients from whom these samples were taken had been or had not been on prescribed doses of digoxin?

A. Well, some had been and some had not been, and I can't -- I don't have that







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tabulated. I don't know. May I refer you to Dr. Phillips, who has all the data on autopsy samples.

Q. Well, will Dr. Phillips be able to tell us how many of the sample group were patients that were on prescribed levels of digoxin?

A. He should be able to, yes. He has that data.

Q. All right.

And can you help us today, Dr. Soldin. Do you know, sitting here today, or in the papers that you have with you today, the sites in the body from which these 37 samples were taken?

A. No, I don't.

Q. And who would be the appropriate individual?

A. Dr. Phillips is the person.

Q. Dr. Phillips?

A. Yes.

Q. Can you tell us again today from the information you have on hand or that you know how soon after death these 37 samples were taken?

A. No.

Let me make it clear. Our laboratory gets autopsy samples which are just numbered and, mostly, we do not get names; we get just a number,





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autopsy number so and so, and then we handle the analysis and then report the results to Dr. Phillips. So, he has essentially all the data. He collects the data, but we don't.

Q. Do I take it then that Dr. Phillips compiled the summary data of the results of all of these tests?

A. Well, he has a summary of all the autopsy results. I'm not sure whether he has the fluorescence polarization results on the autopsy samples.

Q. All right.

A. Because that was a study which we initiated.

Q. Well, are you then, Dr. Soldin, as the biochemist who is overseeing the use of that methodology, are you then in a position today to give us the breakdown of the results on those 37 samples; first on the RIA and then, comparatively, on the FPIA?

A. I can give you the following breakdown; namely, that, by both methods, there were 23 samples that had results of less than 0.5 nanograms per millilitre. There were three samples --





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THE COMMISSIONER: That's less than  
0.5?

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THE WITNESS: Less than 0.5 for  
both methods. There were three samples that had the  
FPIA method - by the FPIA method, sorry, where less  
than 0.5 but by the RIA method ---

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THE COMMISSIONER: Take it slowly.  
FPIA was 3 samples of less than 0.5. I take it those  
are separate from the RIA ones, 3 that were only less  
than 0.5 by FPIA, is that what you are saying?

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THE WITNESS: No. Well, there were  
23. I'm dividing it into separate groups. Now,  
in the first group of 23 samples, both methods read  
less than 0.5.

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THE COMMISSIONER: I got 0.5.

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THE WITNESS: Yes. In the second  
group the RIA method read more than 0.5 and the FPIA  
group method read less than 0.5.

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THE COMMISSIONER: I'm sorry, you  
will have to - it is partly the machine, but I'm  
having trouble listening. The second group - could  
you say that again?

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THE WITNESS: The second group there  
were 3 samples in which the FPIA method read less  
than 0.5 nanograms per millilitre and the RIA method  
read greater than 0.5.

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MS. CRONK: Q. On the same three samples?

A. On the same three samples.

Q. Yes. That takes us up to 26. What about the rest of the samples?

A. There were two samples in which the FPIA method read greater than the RIA method.

Q. Yes.

A. And there were nine samples -- I should qualify that further. Both of those two samples had results greater than .5.

THE COMMISSIONER: Both of those what?

THE WITNESS: Would have results greater than 0.5. So, there were two real readings in other words of what were real measurements.

MS. CRONK: Q. But the FPIA results were higher?

A. Yes.

THE COMMISSIONER: Wait a minute. The FPIA were higher, is that not what you said?

THE WITNESS: In those two samples.

THE COMMISSIONER: Yes, all right. Nine samples.

THE WITNESS: And there were nine samples in which the RIA results were greater than the FPIA result, again, greater than both methodologies





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having resulted greater than 0.5.

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MS. CRONK: Q All right. Then

dealing, Dr. Soldin, with that last category, the  
nine samples in respect of which the RIA reported  
a higher result than was obtained on the FPIA. Can  
you tell me of that nine what the highest two or three  
RIA readings were that you obtained?

A. I believe the highest was 12.9  
nanograms per millilitre.

Q. And how did that compare to the  
FPIA reading on the same sample?

A. It was 7.4 nanograms per  
millilitre.

Q. And for purposes of illustration,  
which was the second highest RIA reading that you  
obtained of those nine?





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A. The second highest was actually on the same patient but drawn from another site. Now I would have to calculate the ---

Q. Well, what was the second highest on a different patient that you obtained on the RIA?

A. On a different patient it was 4.8 RIA nanograms per millilitre and 4.3 by FPIA.

Q. And I take it that inasmuch as you have told us that all nine of those samples had higher RIA readings and in the FPIA corresponding readings were lower, if we went to each of the nine we would just find a similar breakdown, the FPIA result would be lower than the nanogram measurement for the RIA?

A. That is correct.

Q. Now other than that sample group of 37 Dr. Soldin, since the introduction of the FPIA method at the Hospital, you have told us that was in March of 1983, have you had occasion to test any other post mortem samples on both methods for comparative purposes other than those 37?

A. No.

Q. Now looking at the results that you have described to us Dr. Soldin, and looking





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first, I am talking now about the comparative results that you have told us about. Looking first at the ante mortem tests done on patients who were not on digoxin, the five that were cross tested on both methodologies, and as I understand it you have told us that the FPIA results in those samples were lower than on the RIA?

A. That's right, yes.

Q. Now the next group of tests, that is the ante mortem samples from patients who were on digoxin were tested on both methodologies and the mean results as reflected in your memorandum I take it to be relatively the same?

A. Correct.

Q. And the third group of tests that you did on post mortem samples were done on both methods, were from patients who were both on prescribed doses of digoxin, and from patients who were not prescribed digoxin, correct? The ones you have just told us about.

A. The autopsy results?

Q. Yes, I'm sorry, the autopsy results, that is the group of 37?

A. That's right.

Q. And in those instances you have







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told us that on at least 12 samples the results obtained by the FPIA method were lower than the comparative results on the RIA method?

A. Right.

Q. What do those results tell you Dr. Soldin, if anything, about the comparative advantages or disadvantages of both methodologies?

THE COMMISSIONER: Haven't told him anything about the advantages, it would tell him something about the readings, wouldn't it?

MS. CRONK: That would be fair, let me rephrase it Mr. Commissioner.

Q. What do those results tell you with respect to the reliability, or attractiveness of one methodology for digoxin assays versus the other, if anything?

THE COMMISSIONER: I still don't see how the results can tell him. He may have some opinion apart from that, or the results tell him that either one is lower than the other, isn't that right?

MS. CRONK: Well, you put it fairly, Mr. Commissioner.

Q. Dr. Soldin, can you tell us, have you formed an opinion with respect to these





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methodologies on the basis of these comparative studies that you undertook?

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THE COMMISSIONER: If you have formed any opinion other than the fact that one is lower than the other I would be surprised, but perhaps you have. On the basis of these figures I don't know what conclusion you could possibly draw, but there may be something else that you have.

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THE WITNESS: Well the possible conclusion that can be drawn is that if the FPIA method may be somewhat more specific that is a possible conclusion. The results, if we take the patients that we know are not receiving digoxin and the results were lower in the FPIA method, and in the RIA method, that is a possible conclusion. I think it is early in the use in our experience with FPIA to draw a conclusion at this point in time.

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So again on the autopsy results overall the FPIA results are lower than the RIA results. In fact if you plot the nine samples in which the FPIA results are lower than the RIA results, you get a slope for that line of 0.6, which means that the FPIA results tend to be 60 per cent of the comparable RIA result.





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Q. Dr. Soldin ---

THE COMMISSIONER: May I just quarrel with that finding with respect to the FPIA being more specific. It certainly gets a lower reading.

THE WITNESS: Yes.

THE COMMISSIONER: And you say because they were not on digoxin, therefore there should be no digoxin reading. We have been hearing all sorts of evidence that in fact you can have digoxin readings even if you haven't any digoxin in your blood, because that is what the Vancouver study was all about.

THE WITNESS: I know you can get digoxin readings if you don't have digoxin in the blood but that indicates a non-specific method for digoxin.

THE COMMISSIONER: Either that or it indicates some digoxin-like substance that records on the RIA. I don't know, anyway that is the conclusion you have reached?

THE WITNESS: Well, I would agree with you it indicates that there could be a digoxin-like substance that cross reacts with the antibody. Another way of saying that in English is







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that the method is less specific. It is just using your exact same words, am I not getting across to you?

THE COMMISSIONER: No, no, you may well be right. It gives you that comfort in any event, does it, you think the FPIA more specifically demonstrates and works better, and bearing in mind that these children were not, did not have digoxin prescribed for them?

THE WITNESS: There were only five patients in which we have comparisons by both methods in which digoxin was not prescribed, and the FPIA result is lower than the RIA result in that group.

THE COMMISSIONER: I would accept that conclusion if the FPIA method scored zero in all instances for children with digoxin was not prescribed. But if the FPIA method does produce a reading of digoxin, where no digoxin has been prescribed I have some difficulty coming to that conclusion. That doesn't mean your reading of it is better than mine. That is where the problem is. If the FPIA came out with zero then I could accept it, but because the FPIA reading comes out with a figure which isn't zero doesn't it follow that it might well be that the FPIA just doesn't





CC-7

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2 pick up all the digoxin-like substances that this  
3 substance X would be produced apparently in the body  
4 of young children?

5 THE WITNESS: Yes, you are right,  
6 conclusions are correct. It is not picking up as -  
7 it is not measuring whatever compound you are  
8 talking about whether it be substance X, that's ---

9 THE COMMISSIONER: It was measuring  
10 something when nothing exists, wasn't it. However I  
11 won't argue with you any more, probably clearly you  
12 are more qualified than I am to reach a conclusion.  
13 Anyway, that is your conclusion that the FPIA is  
14 more specific?

15 THE WITNESS: My conclusion is a  
16 guarded conclusion. We have little data at the  
17 present time. We have those five patients that we  
18 have done by both methods. We also have the  
19 autopsy data from which we have done some 37 cases  
20 by both methods, now many of the patients in the  
21 autopsy study were on digoxin, right.

22 The FPIA method, taking both these  
23 groups generally came out lower, the results by the  
24 FPIA method, generally came out lower than the RIA  
25 method and so a possible and in fact a probably  
interpretation is that the FPIA method is more





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2 specific.

3 MS. CRONK: Q. Dr. Soldin, you told  
4 us earlier as well that you anticipate as a result of  
5 active consideration of the matter by the Hospital  
6 in the recent past that it is likely within two to  
7 three weeks I believe that was the time frame that  
8 you referred to, that all digoxin assays in the  
9 Hospital would be done on the FPIA as opposed to the  
RIA method. Do you recall giving that evidence?

10 A. Yes.

11 Q. And I take it that the  
12 memorandum which you prepared for Dr. MacLeod and  
13 which we have now marked as an exhibit is your  
14 memorandum to Dr. MacLeod in support of that proposal?

15 A. That is correct. There was a  
16 meeting held subsequent to that memo which was a  
17 meeting with the Medical Director of the Hospital  
18 and some of the administrators, et cetera. Dr.  
19 MacLeod was there, and Dr. Goldberg was there, in  
20 which the decision was made essentially to switch the  
assay from the RIA procedure to the FPIA procedure.

21 This decision was made because of  
22 the data that we had collected as well as because  
23 of data that the AACC, that is the American  
24 Association for Clinical Chemistry Therapeutic Drug  
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CC-9

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2 Monitoring Program has published on the FPIA  
3 procedure and how well that procedure is doing in  
4 the external quality control programs relative to  
5 other procedures.

6 Q. If we look at page 4 of the  
7 memorandum and attachments that you forwarded to  
8 Dr. MacLeod do we find in a typewritten form a  
9 summary of what you consider to be some of the  
10 advantages of moving exclusively to the FPIA  
11 technique for running digoxin assays, together with  
12 some of the disadvantages?

13 A. Yes, that's right, I have a  
14 summary here.

15 Q. And when you refer in the  
16 in the advantages section again, just for the  
17 purposes of clarity to Stat - S-T-A-T - measurements  
18 are you referring there to emergency or urgent  
19 digoxin assay requests?

20 A. I am, yes.

21 Q. And if we look at the last page,  
22 the last attachment to your memorandum Dr. Soldin,  
23 can you explain to us briefly what this data  
24 represents?

25 A. Basically this data is the  
data for April of 1983 published by the American







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Association for Clinical Chemistry and Therapeutic Drug Monitoring Program. There were 404 laboratories that performed digoxin assays in that particular month in this program.

Q. And do we find that indicated close to the bottom of the page on the left beside the words "all labs"?

A. Correct.

Q. All right.

A. There were some 312 in that month that used the RIA technique, and there were some 35 that used the fluorescence polarization-immunoassay technique. You can see that the mean results on this particular quality control sample from both the RIA techniques and by the FPIA techniques was the same.

Q. How do we see that Dr. Soldin?

A. Because under the column "Mean" you get 3.87 for the RIA labs, that is 312 labs.

THE COMMISSIONER: I'm sorry, under what column did you say?

THE WITNESS: The "Mean" column.

THE COMMISSIONER: Thank you.

THE WITNESS: The column is headed





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"Mean". You get 3.87 for the mean result obtained by the RIA laboratories, and you get 3.87 for the mean result for the FPIA laboratories. So the means were the same.

If you look at the standard deviations ---

Q. Which is the next column?

A. Which is the next column, the standard deviations reported by the RIA laboratories was 0.38 which is very close on a 10 per cent coefficient of variation, and the next column shows it was 9.78 per cent X.C.V., so very close to 10 per cent.

In contrast the S.D. in the FPIA laboratories was 0.17 and the coefficient of variation was 4.43.

Q. Do I correctly take that to mean that on the basis of the experience on these laboratories, that is those who were using, during the month of April 1983 the RIA method and the FPIA method, that there was a greater variability results on the RIA assays than there were on the FPIA?

A. That is correct, from this data.

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Q. What does the column headed  
what I take to be "minimum" and the column headed  
"maximum" indicate to us?

A. That should be the minimum  
result obtained and the maximum result obtained by  
all the labs for that particular type technique. So  
the minimum result obtained by the RIA labs was 0.42  
on a sample that should have read around 3.8.

The target value, as you see in the  
far right-hand corner was 3.8.

Q. So we relate the figures in the  
minimum column to the target value of 3.8?

A. Correct. The target value was  
3.8 and the mean result as obtained by the RIA labs  
was 3.87 which was pretty close to the target value  
but the worst laboratory had a result of 0.42, that  
is, the worst laboratory as far as being low is  
concerned; and the worst laboratory as far as  
reporting inaccurate high results was 11.79 so that  
the scatter as you can see - 3.8 was what they should  
have got but the scatter range from 0.4 to 11.79  
in these 312 laboratories.

Q. If you take the 35 labs that  
use FPIA, the mean result was 3.87 which again was  
pretty close to the target of 3.80. The scatter







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was from 3.54 to 4.30 which I think you will agree is a much narrower range and indicates a much tighter control of the assay.

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Q. And those values, I take it, both in respect of the RIA results and the FPIA results reflect a range of error or inaccuracy reported on the assays conducted by that particular technique in that month?

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A. Right.

Q. And those factors as well - or did they - have any relevance to your considerations in preparing this proposal for Dr. MacLeod?

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A. They had some relevance. Obviously we cannot judge our RIA technique by the results produced by other laboratories' RIA techniques especially if their techniques are poor. So we have to compare our precision by FPIA at Sick Children's with our precision at Sick Children's using the RIA technique, and those comparisons remain.

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As you know, our RIA technique is really quite a good technique and our CB's are very comparable using the RIA technique to those obtained by FPIA.

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THE COMMISSIONER: Are you saying that this is some kind of human error?





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THE WITNESS: It is error, whether it is all human error is another issue. It could be - there are a lot of reasons for a laboratory performing poorly on a particular sample. Many of those reasons are human errors.

These were assays done by 312 labs all on the same sample, and it was sent to all these laboratories and some of the labs using RIA techniques perform very poorly. It could be that they were using the wrong RIA kits or poor kits or poor antibodies. There could be many reasons for producing inaccurate results. The question one asks is are those particular laboratories both inaccurate and imprecise? I am talking about the labs that performed poorly.

Q. So that although there could be many reasons leading up to a resulting range of that kind it is the range of error or inaccuracy that is at least one factor that you look to as a measure of the efficiency of the particular technique?

A. Right. What the study is showing is that FPIA is such a simple technique, you can put it in 35 labs and all 35 labs come out with data which is almost the same, whereas the RIA technique is perhaps a little more complicated and in some labs





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they perform well but in quite a few labs they do not.

MS. CRONK: Thank you, Dr. Soldin.

Mr. Commissioner, apropos of our discussion before the break, I met with Dr. Soldin and discussed with him, not in detail, the post mortem testing samples that had been tested for digoxin during the period March 1981 up to April of 1983, that is all on the RIA method and not on the FPIA method.

I am advised by Dr. Soldin and his Counsel that the appropriate individual from whom to obtain information as to the nature of the samples tested and the results achieved is Dr. Phillips.

Dr. Soldin does have some limited, with respect, some limited knowledge as to the results of those tests and he is prepared to give it to us today but he has cautioned me as has his Counsel that --

THE COMMISSIONER: When is Dr. Phillips scheduled?

MS. CRONK: Our hope would be to call Dr. Phillips very close to the time that we intend to recall Dr. Ellis because Dr. Ellis, as you know, will be talking about specific sample testing that he did and the results obtained during the July 1980 to







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2 March, 1981 time frame.

3 It would then be our intention to call  
4 Dr. Phillips to speak to those tests that were con-  
5 ducted from March, 1981 until the introduction of the  
6 FPIA method.

7 THE COMMISSIONER: In any event, I  
8 take it, you are not going to ask him any questions?

9 MS. CRONK: That is not my intention,  
10 sir.

11 THE COMMISSIONER: I suppose I do not  
12 need to cross that bridge until somebody does.

13 MS. CRONK: I have no further questions  
14 at this time of Dr. Soldin, Mr. Commissioner.

15 MR. STRATHY: Then I will raise the  
16 bridge, Mr. Commissioner. It seems clear from the  
17 witness' evidence that there are documents that  
18 reflect the results of the various tests that have  
19 been done.

20 THE COMMISSIONER: Are these the  
21 post mortem results?

22 MR. STRATHY: I understand that they  
23 are both pre-mortem and post mortem, from what  
24 Dr. Soldin has said. I wonder if there is any  
25 reason why those cannot be filed, if not today then  
tomorrow, as exhibits?

MS. CRONK: I have no objection to  
that at all, Mr. Commissioner. It is just that  
in the time available there was not sufficient time  
to copy much of that material.







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THE COMMISSIONER: Is there some possibility we might have those tomorrow?

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MS. CRONK: Yes, I will be glad to undertake to meet with Dr. Soldin and arrange that. I should make it clear however that the documents of which I am aware, the documents that Dr. Soldin has with him, relate to the comparative testing that he conducted, that he has just described.

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MR. STRATHY: I am not talking about just those.

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THE COMMISSIONER: If there are documents available and if they can be produced, I think it certainly would seem to me that that sort of evidence is relevant, but there is no point in having it if the witness does not know anything about it. So I think counsel will just have to use their discretion with respect to that. It is obvious that if the witness does not know as much as he should know about it to give any sensible answers then there is not much point in pursuing it.

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Is that the completion of your --

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MS. CRONK: Yes, Mr. Commissioner. I have spoken to Miss Devins, and Dr. Soldin, within reason, is willing to meet with other counsel, if it will assist them in preparing their cross-examination.





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THE COMMISSIONER: What is the general feeling? Would you prefer to have that sort of session now? If we have that sort of session now we may as well adjourn until tomorrow morning. If, on the other hand, if anybody wants to cross-examine now we will do it that way.

Can we have a sort of a show of hands, if you like, as to who wants to have the informal discussion with Dr. Soldin now? Can we have a show of hands? It looks as though that is fairly well unanimous. So I think that is all right.

Thank you, Dr. Soldin. I will see you tomorrow, and you will be faced with some others almost immediately.

MS. CRONK: Thank you, sir.

THE COMMISSIONER: You will make the arrangements, will you, Miss Cronk?

MS. CRONK: I will, sir.

THE COMMISSIONER: All right. We will rise until ten o'clock tomorrow.

--- Whereupon the Hearing adjourned until 10:00 a.m., Thursday, July 7th, 1983.

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